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THE CASE AGAINST B.C.G.

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Since 1882 numerous attempts have been made to produce immunity artificially in tuberculosis. A large number of preparations have been produced and tried. Some have consisted of living bacilli of various degrees of virulence and types, while others have been composed of fractions of or whole organisms killed by different methods, including heat, electricity, chemicals, etc. None of these preparations has passed the controversial stage. This is probably because an attack of tuberculosis does not result in dependable immunity, so the disease is notoriously a relapsing one.

There are about half a dozen preparations referred to as vaccines now being recommended as immunizing agents in various parts of the world. The one at present in the ascendancy is bacillus Calmette–Guérin (B.C.G.).

As good or better results in tuberculosis control have been reported in parts of the world where only fundamental methods have been employed as in other places where B.C.G. has been added.

The main purpose of this paper is to call attention to various items in the natural history of tuberculosis, and the factors which seem to have been most important in the relatively rapid-changing tuberculosis scene.

It was recently stated that there were approximately 100,000 newly reported cases of tuberculosis in the United States in 1930 and in 1954, inferring that nothing was accomplished in the interim (Medical Advisory Committee of Research Foundation, 1957). The actual figures were 124,940 in 1930, 100,540 in 1954, and 68,866 in 1956—a decrease of 44.9%. In 1930 most of the reported cases were found because they were ill. Presymptomatic lesions in a large number of persons that year were not sought. In 1954 and 1956 the number of cases examined because of symptoms had decreased. To those cases, however, were added many persons whose disease was detected in the pre-symptom stage by periodical examinations, mass surveys, and the like.

More precipitous decreases occurred in mortality. In 1930, 86,142 persons died from tuberculosis—a death rate of 70.2 per 100,000 population; but in 1954 there were only 17,074 deaths and in 1956 14,061 deaths—rates of 10.2 and 8.4 per 100,000. Children and young adults profited most, as they were born after the fundamental protective measures such as sanatoria and control of disease in animals were instituted. Among persons from birth to 24 years, between 1942 and 1946 the annual number of deaths was over 9,000; whereas in 1956, 600 died. In 1942, 2,702 children from birth to 14 years died from tuberculosis, whereas in 1956 there were 290 deaths. The mortality rate decreased more than the case rate because of new methods of treatment, which at least postponed death for many tuberculous persons.

There is an estimated backlog of approximately 56,000,000 persons harbouring tubercle bacilli. These individuals and those whom they may infect provide the new clinical cases. Under present conditions the case rate cannot decrease very fast. In fact, it will depend upon the dwindling of the backlog of infected persons which is taking place by preventing tubercle bacilli from invading the young and by exodus of the older generations, where most of the tubercle bacilli lurk.

Marked decrease has occurred in the tuberculous infection attack rate. Indeed, tuberculous infection in infancy has become relatively rare in most places. Among children of grade-school age, usually not more than 2 to 3% in rural areas react to tuberculin. Even

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in one city of half a million people, infection decreased from 47% among grade-school children in 1926 to less than 4% in 1954 (Myers, Gunlaugson, *et al.*, 1955). In Syracuse, testing of junior high-school students in 1934 revealed 34.7% reactors, but in the school year 1957–8, only 3.7%.

From 1949 to 1951 Palmer *et al.* (1956) tested more than 120,000 white men and women, 17 to 21 years of age, with an intermediate dose of tuberculin. They included Navy recruits from all parts of the United States and students, mostly freshmen, attending colleges and universities in 17 states. Only 8.8% reacted.

On the basis of actual tuberculin-testing in a few counties, it has been estimated that about one-third of the people of the United States are harbouring foci of tubercle bacilli. Most of these persons are 40 years or older. In a county-wide tuberculin-testing survey in Minnesota, Jordan and Jordan (1954) found 50.8% of women and 59.3% of men between 60 and 69 years old reacted to tuberculin. As children they were provided little or no protection against tubercle bacilli. It is they who are now contributing the bulk of morbidity and mortality from tuberculosis. In the entire state in 1957, the tuberculosis mortality rate was 3.1 per 100,000. However, 85% of the deaths were in persons 40 years or older and 52% were 60 or older. From birth to 24 years only four (4.8%) deaths occurred. There were corresponding morbidity percentages in the various age groups.

Inasmuch as most B.C.G. proponents recommend it only for those uninfected, it would not be applicable to the approximately 56,000,000 citizens in the United States who already are tuberculin reactors. Moreover, among the remainder the tuberculous infection attack rate has reached such a low ebb that relatively few would be expected to become infected—and it is still decreasing. Furthermore, treatment now available is effective for recently developed clinical lesions.

Veterinarians of Canada and the United States put B.C.G. to most rigid tests among the cattle herds in the late 1920s and early 1930s, but they found it neither practical nor efficacious. In some other areas of the world B.C.G. has been abandoned as a part of the tuberculosis eradication programme. International organizations dealing with livestock diseases in Europe, including the International Office of Epizootics, the World Health Organization, and the Organization for European Economic Co-operation, recognize the incompatibility of B.C.G. vaccination with proved methods of control based upon use of the tuberculin test. These bodies are on record as recommending that such products as B.C.G. and vole bacillus be omitted from control programmes designed for eventual eradication of bovine tuberculosis (O.E.E.C., 1952).

Specificity of the Tuberculin Reaction

From 1908 to 1912 Anton Ghon (1916) did careful necropsies on the bodies of 184 children who during life showed no evidence of tuberculosis except reactions to the epidermal tuberculin test (Pirquet). Tuberculous lesions were found in 183 (one was not completely examined). He said: "From the standpoint of the pathological anatomist, my researches, which in regard to the question is not limited to the cases described here, justify me in concurring entirely with those who advocate the specific value of the tuberculin reaction." The millions of necropsies on tuberculin reactor animals have also supported the specificity of the tuberculin reaction (Steele and Ranney, 1958).

Of the various phases of examination, only the tuberculin reaction and the recovery of tubercle bacilli are specific for tuberculosis.

Other Values of the Tuberculin Reaction to be Preserved

The tuberculin test is exceedingly important in differential diagnosis. It determines earlier than any other procedure when tubercle bacilli have invaded the body. It is the best epidemiological agent. It determines the effectiveness of tuberculosis control measures far earlier and more accurately than other criteria. It determines responsibility in tuberculous cases that come to litigation. There is the hope that anti-tuberculosis drugs will be found to cure tuberculosis in the sense of destroying all tubercle bacilli if they are administered with reasonable promptness after the invasion occurs. At that time, lesions are microscopic and vascular, so drugs in the blood stream may reach all tubercle bacilli. If time lapses so that the characteristic loss of blood supply to lesions has occurred, the hope of reaching all tubercle bacilli with drugs in the blood stream is forfeited.

These and other uses of the test are lost to persons whose tissues are sensitized to B.C.G. tuberculoprotein. Concerning the possibility of differentiating between reactions caused by B.C.G. and those by natural infection, Quaiser (1954) said: "It is impossible to distinguish between the tuberculin sensitivity produced by natural infection and that produced by B.C.G. vaccination by means of the intracutaneous tuberculin test with old tuberculin or even with B.C.G. tuberculin."

Veterinarians of Canada and the United States reported that B.C.G. destroyed the use of the tuberculin test, which is their best diagnostic agent. They continued with this test to screen infected animals to be removed from herds. From 1917 to 1958, in the United States, they administered the test to cattle 396,687,286 times and did necropsies on 4,077,995 reactors (U.S. Department of Agriculture, 1959). This programme cost approximately $326,000,000, but on the basis of current prices it has saved more than $150,000,000 annually. Thus, every two years nearly as much is saved as the entire 40-year programme cost (Steele and Ranney, 1958).

Many more millions of tests have been administered in other parts of the world, indicating the confidence veterinarians have in the specificity and accuracy of the tuberculin reaction.

Initial Invasions with Tubercle Bacilli

Krause (1928), Vorwald (1932), and Lemon and Montgomery (1934) demonstrated that when tubercle bacilli are introduced subcutaneously direct into the pleural space, and into the blood stream of animals, they soon appear in other parts of the body, including those remote from the site of administration. Nearly always some of these bacilli become deposited in the lungs, while others are focalized in various extrathoracic locations. In fact, Ravenel and Reichel (1908) and Calmette (1923) found that when tubercle bacilli are introduced direct into the gastro-intestinal tract of animals, some soon appear in the lungs.

Establishment of Primary Tuberculosis Complexes

Vorwald (1932) has shown that lesions start to form within an hour after tubercle bacilli are introduced into

the bodies of animals. Wallgren (1955) found that when tubercle bacilli invade the bodies of infants it requires about three to seven weeks before sensitivity to tuberculoprotein is demonstrable. In people, primary tuberculosis complexes are well established by the time sensitivity to tuberculoprotein can be elicited by the tuberculin reaction.

When allergy can first be elicited by the tuberculin reaction the primary pulmonary infiltrate cannot be located by any phase of an examination in approximately 95% of the cases. This is because the infiltrates do not have consistency or are not large enough to cast visible shadows on *x*-ray films, or they are located in the 25% of the lungs not visualized on the usual postero-anterior *x*-ray film or are extra-thoracicly located. In the remaining 5% of cases primary pulmonary infiltrates have size, consistency, and location to cast shadows on *x*-ray films of the chest.

When B.C.G. is effectively introduced into the layers of the skin it sets up lesions at the site of administration and in the regional lymph nodes. When allergy can first be elicited many lesions in the skin are too deep or too small to appear significant and the involved lymph nodes are not palpable. In others the skin lesions are larger, and the regional lymph nodes are palpable. In some, much larger lesions appear in the skin which break down and discharge pus, while regional lymph nodes become markedly enlarged and may rupture.

It was formerly believed that B.C.G. has a fleeting existence in animal and human bodies, but Gernez-Rieux *et al.* (1950) administered it to guinea-pigs by the scarification method and regularly recovered organisms from the skin lesions on the 41st and occasionally on the 79th day. Regional lymph nodes revealed bacilli on the 175th day. Vorwald *et al.* (1954) found living bacilli for at least 18 months in silicotic guinea-pigs. B.C.G. is also carried from the site of administration to lymph nodes and internal organs a short time after administration. Ström (1950) observed that some bacilli administered intracutaneously reached the nearest lymph node 18 cm. distant in three minutes, and about half had arrived at this point in 10 minutes. Gernez-Rieux *et al.* (1950) found organisms in the spleen on the 11th day.

It appears, therefore, that tubercle bacilli of the initial invasion, whether they are from natural infection or from introduced B.C.G., take essentially the same course with reference to distribution and with the formation of primary lesions. All who develop sensitivity to tuberculoprotein, whether from natural or B.C.G. infection, have primary tuberculosis complexes. Apparently the only significant difference in the two groups is that the one is produced artificially in the skin and the other appears naturally, especially in the lungs. It does not seem reasonable to give those in the lungs a different classification from those produced in the skin and regional lymph nodes. Demonstrable primary infiltrates in the lungs usually come under control spontaneously, as do corresponding B.C.G. lesions in the skin.

Demonstrable primary pulmonary infiltrates from natural infections vary in size from those scarcely large enough to be visualized on *x*-ray film to large dense homogeneous areas. Indeed, the shadows they cast may suggest extremely serious and extensive clinical disease. In some cases acid-fast bacilli may be recovered from gastric washings for a brief time, and occasionally they result in haemoptysis. Before there had been opportunity to conduct longitudinal studies on such lesions, drastic treatment was nearly always recommended. However, when an opportunity came to observe a group of children with such lesions under varying conditions they were found to be benign, and they resolved over the course of a year or more, leaving only evidence of Ghon tubercle formation at the former site of the pulmonary infiltrate and/or evidence of calcific deposits in the regional lymph nodes.

In fact, Myers *et al.* (1935) strongly recommended institutional care for all children who had demonstrable primary pulmonary infiltrates. Some families permitted their children to be admitted; others refused, but allowed their children to attend a special day school; while other families refused both institutions, and their children remained at home. When traced later, all the primary pulmonary infiltrates had resolved in the same manner regardless of how much or how little treatment was administered.

The report (Myers *et al.*, 1935) contained the following statement: "Therefore, the immediate prognosis of tuberculosis of the first infection type among children and young adults is excellent either in the absence or presence of treatment."

When in 1920 one of us began longitudinal observations on persons infected with tubercle bacilli (Myers, 1927, 1933), there was a widespread belief that if the initial infection were postponed to young adulthood it would result in much more serious and rapidly progressive disease than when acquired in childhood. There were those who expressed great fear of this situation, believing that infections postponed to the teenage period or later would be exceedingly hazardous.

However, no report was found of a longitudinal study of a group of individuals to determine just when their infections had occurred and the sequence of subsequent events. There was no doubt about the destructiveness of pulmonary tuberculosis in girls and boys in the teenage period. In fact, in the state of Minnesota 200 or more died from tuberculosis annually. As late as 1942–6 more than 3,000 girls and boys from 10 to 19 years old died annually in the United States. Longitudinal observations which began in 1920 offered some promise of determining whether the destruction in the teenage period occurred among those recently infected. Sizable numbers of children, tuberculin reactors and non-reactors, were observed as they entered and passed through the teenage period along with groups of students of nursing and medicine whose tuberculin sensitivity status was determined on admission to school, and the non-sensitive individuals were tested periodically to determine if and when infections with tubercle bacilli were acquired.

By 1937 enough young adults had become infected under our observation and were observed, so that a report containing the following seemed justified (Myers *et al.*, 1937):

"In a small percentage of those who in adult life become contaminated for the first time, the focus of the disease when located in the pulmonary parenchyma attains sufficient size to cast a shadow on the *x*-ray film which can be visualized by the naked eye. Such shadows usually become visible during the first three or four months after the infection has occurred. When these shadows reach their maximum size, they may show the same general appearance over a period of many months, after which they gradually

recede. In some cases, the shadows remain, revealing evidence of fibrous and calcium deposits, while in others they completely disappear.

"The first infection type of tuberculosis as observed in our group of adults has resulted in no significant symptom or abnormal physical sign throughout the entire course of development. Indeed, the lesions in the majority of our cases would not have been known to exist had it not been for periodic tuberculin-testing and the making of roentgenograms of the positive reactors.

"In our experience, adults in whom the first infection type of tuberculosis develops, even with considerable involvement of the pulmonary parenchyma and regional lymph nodes, do not require treatment in any form."

Twenty years later (Myers, 1957), 2,315 persons were reported who were observed to convert from non-reactors to reactors to tuberculin in adulthood, of whom 15 had died from non-tuberculous conditions, and 34 had not recently been traced. The remaining 2,266 had 27,099 person-years of follow-up.

Of the 2,266, there were 2,080 with 24,431 person-years of follow-up who had no demonstrable tuberculous lesion.

Among the remainder, 54 presented demonstrable primary pulmonary infiltrates about the time they were found to be sensitized to tuberculin. They had been observed from 2 to 25 years since the primary infiltrates were first seen and had a total of 749 person-years of follow-up. Five (9.3%) subsequently developed clinical tuberculosis from 1 to 10 years after the primary infiltrates were first in evidence. In the entire 54, the demonstrable primary pulmonary infiltrates gradually resolved over a period of one year or more, with no evidence of clinical disease in the areas they had occupied.

Among the 2,266 traced, another group of 67 developed pleurisy with effusion of whom 14 had coexisting demonstrable primary infiltrates. There was a follow-up of 932 person-years. Of the nine who had pleurisy with effusion but later developed clinical lesions, only two had presented demonstrable primary pulmonary infiltrates. These resolved in the usual way.

Thus no case in this entire group of 2,266 persons who acquired primary tuberculous infection in adulthood developed rapidly progressive fatal disease.

Differentiation Between Primary Infiltrates and Clinical Lesions Imperative

Inasmuch as primary pulmonary infiltrates (both demonstrable and non-demonstrable) are so benign, it is imperative that the demonstrable ones be differentiated from chronic reinfection (clinical) type of tuberculous lesions which cause so much illness and death. Primary pulmonary infiltrates resulting from natural infections are the initial inflammatory stage of Ghon tubercle formation.

X-ray shadows are not pathognomonic, and even when they are cast by tuberculous lesions one cannot differentiate between primary infiltrates and those due to reinfection (clinical) types of lesions. It is only when a series of tuberculin tests have been administered and recent conversion has occurred that the primary infiltrate can immediately be differentiated from the reinfection type of clinical lesion. If such tuberculin testing has not been done before a primary infiltrate is discovered, it can be identified only by a period of observation with serial *x*-ray films. This usually requires a year or more.

Although primary pulmonary infiltrates have hilum lymph-node components, McPhedran's (1927) careful studies revealed that it is not possible to detect lymph-node enlargements on *x*-ray films unless they extend towards the periphery and encroach upon the lung parenchyma. Many lymph-node components of primary tuberculosis complexes do not attain such size; therefore the absence of shadows in differentiating between primary infiltrates and clinical lesions is not helpful.

Immediate Danger of Natural Primary Infection Overemphasized

In pre-vaccination campaigns the impression has sometimes been left that most uninfected children and young adults are in great immediate danger if infection should occur. From May, 1921, to November, 1941, 813 infected children ranging in age from birth to 5 years were observed (Torres *et al.*, 1944). Among them were 102 (12.54%) who presented demonstrable primary pulmonary infiltrates, all of which subsided in the usual manner. Of the 813, only 11 (1.35%) developed acute, fatal reinfection forms of disease and another 11 later developed chronic reinfection type of lesion in bones, joints, lymph nodes, etc. Over a 20-year period beginning in 1921, 6,823 children from 6 to 14 years of age were examined (Harrington, 1944). Of the 2,979 who reacted to tuberculin, 137 (4.6%) had or subsequently developed tuberculosis of reinfection type. The majority had chronic extrathoracic lesions.

Thus, among 3,810 tuberculin reactor children from birth to 14 years, 3,651 developed no evidence of clinical disease. If B.C.G. had been administered before natural infection, it might have been given credit for preventing clinical disease in these 3,651 children.

From May, 1921, to November, 1941, among more than 19,000 children examined, 300 had demonstrable primary pulmonary tuberculous infiltrates (Myers, 1959). Among the 267 recently traced, 10 stated that they were in good health, but have not yet been re-examined. Twenty-six had died. Nine of the deaths were due to tuberculosis, of which seven were caused by meningitis, miliary disease, and pneumonia soon after the infections occurred, and the primary pulmonary lesions were in evidence. The remaining two died from chronic pulmonary tuberculosis 8 and 13 years after the primary pulmonary infiltrates were first found. Among the 241 traced survivors (10 not recently examined), nine had developed chronic clinical types of tuberculosis. One appeared five years after the primary pulmonary infiltrate was seen, one 7 years, one 9 years, two 11 years, one 15 years, one 25 years, and two 27 years. Seven of these cases had pulmonary lesions, one bronchial, and one renal. All were treated successfully.

The surviving traced and examined 231 have had 6,009 person-years of follow-up. No evidence of clinical tuberculosis had developed in 222.

Most of the morbidity and mortality reported in the above studies occurred approximately two decades ago. By fundamental protective measures in the same city, case and mortality rates decreased so that in 1956 only 17 cases were reported among persons under the age of 20 years (of which only five were clinically significant), and no one under the age of 35 years died from tuberculosis (Myers, 1959). If B.C.G. had been administered it might erroneously have been given credit for this accomplishment.

Long-term Hazard of Primary Infection Emphasized

To avoid erroneous deductions with reference to efficacy of therapeutic and preventive measures, it is of extreme importance to recognize the demonstrable primary pulmonary infiltrate. However, its benignity affords no security regarding subsequent acute and chronic clinical forms of tuberculosis. While it has not been demonstrated that the 5% of persons with demonstrable primary infiltrates later develop clinical disease more frequently, percentage-wise, than the 95% with non-demonstrable primary infiltrates, it should be emphasized that all persons with primary tuberculosis as manifested by the tuberculin reaction should be examined periodically for possible evolving clinical lesions.

The individual who reacts to tuberculin is likely to have not only primary pulmonary infiltrates, but also focalization in other locations. Thus, the reactor may have clear *x*-ray films of the chest but develop tuberculous meningitis from lesions of short or long standing in or adjacent to the central nervous system, as demonstrated by Rich and McCordock (1933). Another individual with clear *x*-ray films may have several lesions appear or clinical pulmonary disease evolve at any time after allergy is established.

Levine (1950) made a follow-up study of 1,165 persons, of whom 601 had received B.C.G. during infancy and 564 had been followed from infancy as controls. Two who had received B.C.G. in infancy had developed reinfection type of pulmonary tuberculosis. This had occurred in none of the controls. He said: "There is no evidence to indicate that B.C.G. given in infancy is capable of preventing reinfection tuberculosis in adolescence."

Long ago it was demonstrated that chronic contagious clinical tuberculosis evolves only among those whose tissues are sensitized to tuberculin. More recently, in four areas where B.C.G. studies were in progress, Palmer and Shaw (1953) found that 286 of the total of 335 cases of demonstrable tuberculosis occurred among those who were reactors at the beginning of the study. Of the remaining 49, it apparently was not determined how many were only demonstrable primary pulmonary infiltrates which one may expect to observe in approximately 5% of recent tuberculin converters.

If tuberculosis eradication is the consideration, mass B.C.G. administration campaigns, as well as those for special groups, are puzzling, because time, effort, and funds are spent upon the non-reactors to tuberculin. Among them there is no present tuberculosis problem. The belief that uninfected persons develop rapidly progressive disease within one or two years after becoming infected and thus create the serious contagious clinical problem has not been verified on a long-term basis.

To spend time, effort, and funds on individuals who have not been infected and many of whom will not be, while the infected are allowed to produce a constant crop of clinical and contagious tuberculous persons disseminating tubercle bacilli among their associates, is bad economy.

Unavoidably Exposed Groups

Inasmuch as B.C.G. administration has been strongly recommended for "unavoidably exposed groups," including students of nursing and medicine attention must be called to results of protective measures without B.C.G. reported by Myers, Diehl *et al.* (1955). Prior to and during the 1920s, clinical tuberculosis was a serious problem among their professional students. A programme was developed which consisted of testing all entering students with tuberculin. Those who reacted were examined promptly and thereafter periodically, including inspection of the chest by *x*-ray films. This screened out those who had clinical pulmonary disease on admission and discovered those destined to develop such disease during their school years. Non-reactors on admission were retested with tuberculin periodically. For those who converted while in school the sources were immediately sought, and were often found in pathological and bacteriological laboratories, in post-mortem rooms, in affiliated hospitals and sanatoria, on various services in general hospitals, and among personnel members. In this manner it was learnt which hospitals and departments were permitting materials and patients to infect students, and this knowledge led to the correction of the situations or the abandonment of such teaching services. Rigid contagious-disease technique was introduced where, in line of duty, students came in contact with known cases of contagious tuberculosis. Patient-admission examinations for tuberculosis and pre-employment examinations of all personnel, with subsequent periodic examinations, were instituted.

Among the graduates in the classes from 1919 to 1932 in the School of Medicine, a survey reported in 1941 revealed that 92 had developed demonstrable tuberculosis and 11 had died while in school or after graduation; whereas, after the programme was well under way, among those who graduated from 1943 to 1957 only one presented a clinical lesion large enough to cast a visible shadow on an *x*-ray film. This occurred a decade ago in a student who was a tuberculin reactor on admission to school.

In a school of nursing where 12 to 19% of the students developed demonstrable tuberculous lesions before these protective measures were introduced, only four have since presented clinical pulmonary tuberculosis, each of whom reacted to tuberculin on admission to school (Myers, Boynton, and Diehl, 1955).

Had B.C.G. been employed in these schools, obviously it would not have been administered to the one student of medicine and the four students of nursing who developed clinical lesions, since they had been naturally infected before admission. Moreover, the large number of non-reactors would have received B.C.G. to no avail, but it could have been erroneously concluded that they were protected by this culture.

To speak of "unavoidable exposure" groups is a reflection on the administration and professional staff of any hospital or professional school. The precedent has been established for almost complete solution of the problem by a method based on sound principle and practice with unquestioned efficacy.

Importance of Accurate Diagnosis and Prolonged Control

Literally hundreds of papers have been published on B.C.G., many of which—in fact, the majority—contain favourable statements. However, a carefully controlled study has never been conducted comparable to what has always been demanded by way of control in other

fields. There has been failure to differentiate between primary tuberculosis infiltrates (Ghon tubercles in the inflammatory stage) and clinical tuberculosis. Other factors operating at the same time have been overlooked, and even with unsatisfactory control no study has been conducted long enough to justify favourable conclusions.

In a large number of reports the only evidence presented pertains to conversion to sensitivity to tuberculoprotein. From that alone it was assumed that the recipients were protected. In another but smaller group, efficacy was based largely on seeing more *x*-ray-shadow-casting lesions in the lungs of controls than in those infected with B.C.G., with no differentiation between primary infiltrates and clinical lesions.

The observations of Aronson *et al.* (1958) on American Indians which began about 1936 revealed more shadow-casting lesions and more deaths in the controls. In one of the reports the following statement appears: "Principally, the information for the analysis consists of annual observations on the tuberculin reaction and annual *x*-ray films of the chests with only limited clinical and laboratory data." Apparently, diagnoses were made largely from *x*-ray shadows. Presumptive diagnoses from shadows are temporarily allowable in practice but have no place in research reports, where diagnosis must depend upon bacteriological findings and where information must be factual for world-wide dissemination. The favourable effect of B.C.G. claimed by Aronson *et al.* becomes less impressive when it is known that better results have been achieved among American Indians in a state in which B.C.G. played no part. In that state the mortality rate among Indians decreased from 529 per 100,000 in 1937 to 0 in 1955.

The alleged efficacy of the numerous agents intended to protect against clinical tuberculosis, both past and present, has differed little. It has been reported that about four or five times more tuberculosis has developed among controls than among the vaccinated. The number of primary pulmonary infiltrates that attain *x*-ray-shadow-casting proportions soon after natural initial invasion occurs is sufficient to account for a considerable part of this difference.

The report of the Tuberculosis Vaccines Clinical Trials Committee of the Medical Research Council of Great Britain (1956) concerned 13,300 adolescents who were non-reactors to tuberculin and served as controls; 14,100 who were non-reactors and received B.C.G., and 6,700 non-reactors who were given vole bacillus. In selecting these groups there were 8,200 examined who already reacted to tuberculin and were observed for subsequent developments. At the time this report was completed the participants had been in the study for two and a half years.

The annual incidence of demonstrable thoracic and extrathoracic lesions in the controls was 1.94%, in the B.C.G. group 0.37%, and in the vole bacillus group 0.44%. The lower figures, which are statistically significant, in the last two groups were thought to indicate that B.C.G. and vole bacillus conferred a substantial degree of protection against tuberculosis. However, the pulmonary lesions were not less extensive or severe in those who had received B.C.G. or vole bacillus. How many of the pulmonary lesions in the control group were only primary infiltrates is not known. Among the 13,300 controls, 756 (5.7%) had become tuberculin reactors on the second test, three to five months after the initial one. This is the time in the natural history of tuberculosis when demonstrable pulmonary lesions are in evidence. Grouping of primary pulmonary infiltrates with clinical lesions provides a number large enough to appear statistically significant, whereas accurate differential diagnosis would probably reduce the number of clinical cases below this level.

The study of the Tuberculosis Vaccines Clinical Trials Committee is designed for a prolonged period. A fine opportunity exists to introduce accurate differential diagnosis and thus make a contribution previously unparalleled. If anti-tuberculosis drugs are administered to each person who presents an *x*-ray shadow, however, it may be impossible to obtain the desired information. Apparently these drugs have little or no effect on demonstrable primary pulmonary infiltrates. On the other hand, they usually significantly hasten resolution of clinical lesions and cause them to take the same course as primary infiltrates do naturally.

No group of B.C.G. recipients have been followed long enough to justify conclusions concerning efficacy. Such outstanding workers as the Oxford University investigators of the vole tubercle bacillus vaccine, Medlar, and others saw the impossibility of conducting a well-controlled follow-up study among people. In fact, the Oxford group, headed by A. Q. Wells, said: "To plan a controlled experiment in tuberculosis vaccination in man is a matter of so much difficulty as to be virtually impossible."

The Calmette-Guérin Organism

Ravenel (1902) said: "We are certain that the various types of tubercle bacilli known to us have sprung from a stock common to them all, and that they have acquired their racial peculiarities by residence in different animals through which they are subjected to a difference in food, temperature, and resistance. In other words, the struggle for life is carried on in the various species of animals under varying conditions, the results being that in each animal the tubercle bacillus acquires properties which best enable it to carry on life in that particular host."

Sweany (1956) says: "The other drawback to antimicrobial therapy is due to that fundamental law of nature, the ability of living species to adapt to changing environment by the survival of mutants when changing environment threatens to exterminate the parent species. Molecular rearrangement within the genes (genotypic changes) result in variations in the offspring that are better adapted to the new condition. . . . The end product of the tubercle bacillus (as well as all other species of living organisms) is therefore the end result of a rigid selection of mutants to fit environments in which they are obliged to grow. . . . In spite of the fact that the tubercle bacillus has appeared to be a rather stable parasite, many variations have been observed since its discovery involving among other changes, variations in morphology, virulence, chromogenesis, and gross colony formation."

The bacillus which Calmette studied and later designated bacillus Calmette-Guérin (B.C.G.) would not produce tubercles in animal tissue. Therefore he regarded it as safe when introduced into humans and referred to it as a *virus fixé*. As time passed, however, it was observed that, when introduced subcutaneously

and later intracutaneously, tuberculous abscesses and ulcers sometimes formed at the sites of administration and the regional lymph nodes enlarged, broke down, and discharged pus. These and lesser visible local lesions occurred often enough to be annoying, and constituted good evidence that changes had occurred in the culture.

Petroff *et al.* (1929) dissociated B.C.G. into two "R" and "S" colonies, with the "S" colony invariably producing progressive tuberculosis in guinea-pigs and occasionally in rabbits. Jensen (1946), of Copenhagen, pointed out that the cultures available in Scandinavia at the end of the second world war varied appreciably with reference to the severity of the skin lesions which they could elicit in guinea-pigs. Dubos (1949) said: "Similarly, it has been observed in our laboratory that three strains of B.C.G. obtained from American collections differ significantly in their ability to produce pulmonary lesions in mice following intravenous injections." Concerning the culture he said, "There is no doubt that it has undergone considerable variations in the course of its long career. Indeed, it would be very surprising if it had not." The cultures he and co-workers studied were mixtures of different bacterial forms and differed in properties such as extent of multiplication *in vivo* in experimental animals.

In cultures obtained from various laboratories, Suter *et al.* (1951) found that none consists of a single bacterial form such as Calmette and Guérin produced. Each culture was composed of multiple bacterial forms which differed in many of their properties. It was found that a culture introduced into mice on deficient diet resulted in progressive and sometimes killing pulmonary tuberculosis (Dubos, 1949). It was also observed that the culture maintained and highly recommended for humans by the Research Foundation of Chicago regularly caused progressive and highly fatal tuberculosis in silicotic guinea-pigs (Vorwald *et al.*, 1954). Hauduroy and Rosset then reported that the culture they employed regularly caused widely disseminated and killing disease in normal golden hamsters (1951) and ground squirrels (1953).

Reports began to appear of serious clinical tuberculosis developing in various organs of people remotely located from the sites of administration. In some groups, particularly infants, a higher percentage of cases developed lesions than others. For example, Hsing (1954) said, "The result of B.C.G. vaccination in newborn babies was alarming and is a matter causing great concern." In 23.3% of his cases lymph nodes ruptured. In other reported groups, such lesions have developed in much smaller numbers, down to 1% or less. Finally, Scandinavian physicians made careful necropsies and concluded that B.C.G. was responsible for fatal tuberculosis in humans (Hollström and Härd, 1953; Meyer, 1954; Thrap-Meyer, 1954; Falkmer *et al.*, 1955). Although only four of these cases have been reported it is not known whether others may have had the same experience, because, in areas where most B.C.G. has been administered, in 38 nations there has been no satisfactory follow-up.

It is stated that with the advent of a freeze-dried preparation of B.C.G. it is now possible to standardize completely the viability, potency, and sterility, as well as to determine its safety before distribution (Medical Advisory Committee of Research Foundation, 1957). This is what Calmette and Guérin believed when in 1924 they designated their culture a *virus fixé*. It is what producers and distributors have claimed for their cultures throughout the decades preceding the freeze-dried era. However, the numerous changes already described, varying from culture to culture, occurred. When Calmette and Guérin's culture was considered a *virus fixé*, it had been under observation longer than the freeze-dried preparation has been available.

The freeze-dried material is still composed of living tubercle bacilli, and it has yet to be proved that they will take a different course on prolonged growth in human or animal tissues than has been observed with cultures derived from the original Calmette-Guérin culture.

Calmette's advice to the effect that living tubercle bacilli which cause tubercle formation in animal tissue should never be introduced into the human body is as pertinent to-day as when it was offered.

Summary

Tuberculosis differs from smallpox in that an attack does not result in dependable immunity. Thus there is slim premise for attempting to produce immunity artificially. Allergy to tuberculoprotein is not an indication of immunity, but is prerequisite to the development of clinical tuberculosis. The human body defends itself better against first invasions with tubercle bacilli than it does against reinfections. Clinical disease develops only in persons who have been previously sensitized to tuberculoprotein.

Accurate differentiation between primary pulmonary infiltrates and reinfection type of clinical lesions is of the utmost importance. Without this, erroneous deductions are made with reference to efficacy of B.C.G. For example, it may be credited with beneficial effects when primary infiltrates are grouped with reinfection type of lesions, so it appears that more control subjects develop clinical disease than those who have primary lesions produced in the skin by B.C.G.

An adequately controlled study of B.C.G. among people living in their homes has never been accomplished. It has been found impossible. However, well-controlled studies were conducted among cattle in North America and elsewhere. B.C.G. failed and was abandoned. In the few places where it is still used with major dependence upon it, tuberculosis remains a serious problem among cattle.

Among people, the most phenomenal accomplishments in tuberculosis eradication have been achieved where little or no B.C.G. has been used, including Iceland, Hawaii, and the Netherlands. In countries which have employed B.C.G. extensively, including Denmark, Norway, and Sweden, marvellous results have been achieved, but along with B.C.G. they have employed the same fundamental methods which alone brought about the most phenomenal accomplishments in history. This also applies to special groups such as students of nursing and medicine.

The numerous values of the tuberculin test in diagnosis, epidemiology, etc., are lost to persons whose tissues have been sensitized to tuberculoprotein by B.C.G.

Bacteriological investigations have revealed that cultures designated B.C.G. were not composed of just one, but of multiple bacterial forms, some of which were definitely invasive for animal tissues. No two cultures were alike. Evidently different mutants and changes had occurred in each of the cultures studied.

Apparently mutants produced destructive disease in animals on deficient diet, those which were silicotic, and at least two species of normal animals. In people, they sometimes caused lesions at the site of administration and of regional lymph nodes, as well as other organs, and death in at least a few cases. Calmette repeatedly warned that no living organism capable of producing tubercles in animal tissues should be administered to people.

If methods of preventing mutation in cultures have been or can be devised, there is no assurance that it will not occur after the living organisms are introduced into human tissues.

REFERENCES

Aronson, J. D., Aronson, Charlotte F., and Taylor, Helen C. (1958). *A.M.A. Arch. intern. Med.*, **101**, 881.
Calmette, A. (1923). *Tubercle Bacillus Infection and Tuberculosis in Man and Animals*. Williams and Wilkins, Baltimore.
Dubos, R. J. (1949). *Amer. Rev. Tuberc.*, **60**, 670.
Falkmer, S., Lind, A., and Ploman, L. (1955). *Acta paediat. (Uppsala)*, **44**, 219.
Gernez-Rieux, C., Sevin, A., and Verschoote, G. (1950). *Ann. Inst. Pasteur (Lille)*, **3**, 103.
Ghon, A. (1916). *The Primary Lung Focus of Tuberculosis in Children*. Churchill, London.
Harrington, F. E. (1944). *The Evolution of Tuberculosis*. Division of Public Health, Minneapolis, Minnesota.
Hauduroy, P., and Rosset, W. (1951). *C.R. Acad. Sci. (Paris)*, **232**, 445.
—— —— (1953). *Experientia (Basel)*, **9**, 267.
Hollström, V. E., and Hård, S. (1953). *Acta derm.-venereol. (Stockh.)*, **33**, 159.
Hsing, C. T. (1954). *Bull. Wld Hlth Org.*, **11**, 1023.
Jensen, K. A. (1946). *Acta tuberc. scand.*, **20**, 1.
Jordan, Kathleen B., and Jordan, L. S. (1954). *Dis. Chest*, **26**, 528.
Krause, A. K. (1928). *Amer. Rev. Tuberc.*, **18**, 208.
Lemon, W. S., and Montgomery, L. G. (1934). *J. thorac. Surg.*, **3**, 612.
Levine, M. I. (1950). *Pediatrics*, **6**, 853.
McPhedran, F. M. (1927). *Amer. J. med. Sci.*, **173**, 245.
Medical Advisory Committee of Research Foundation (1957). *J. Amer. med. Ass.*, **164**, 951.
Meyer, J. (1954). *Amer. Rev. Tuberc.*, **70**, 402.
Myers, J. A. (1927). *Tubercle (Lond.)*, **8**, 515.
—— (1933). Ibid., **14**, 212.
—— (1957). *Dis. Chest*, **31**, 384.
—— (1959). *Amer. Rev. Tuberc.*, **79**, 19.
—— Boynton, Ruth E., and Diehl, H. S. (1955). *Dis. Chest*, **28**, 610.
—— Diehl, H. S., Boynton, Ruth E., and Horns, H. L. (1955). *J. Amer. med. Ass.*, **158**, 1.
—— —— —— —— and Trach, B. (1937). *Arch. intern. Med.*, **59**, 1.
—— Gunlaugson, F. G., Meyerding, E. A., and Roberts, Jean (1955). *J. Amer. med. Ass.*, **159**, 185.
—— Harrington, F. E., Stewart, C. A., and Wulff, Marjorie (1935). *Amer. Rev. Tuberc.*, **32**, 631.
Organization of European Economic Co-operation (1952). The Control of Livestock Diseases in European Countries. Technical Assistance Mission, No. 63. Paris.
Palmer, C. E., Krohn, E. P., Manos, N. E., and Edwards, Lydia B. (1956). *Publ. Hlth Rep. (Wash.)*, **71**, 633.
—— and Shaw, L. W. (1953). *Amer. Rev. Tuberc.*, **68**, 462.
Petroff, S. A., Branch, A., and Steenken, W., jun. (1929). Ibid., **20**, 275.
Quaiser, K. (1954). *Beitr. Klin. Tuberk.*, **110**, 507.
Ravenel, M. P. (1902). *Univ. Penn. med. Bull.*, **15**, 66.
—— and Reichel, J. (1908). *J. med. Res.*, **18**, 1.
Rich, A. R., and McCordock, H. A. (1933). *Bull. Johns Hopk. Hosp.*, **52**, 5.
Steele, J. H., and Ranney, A. F. (1958). *Amer. Rev. Tuberc.*, **77**, 908.
Ström, L. (1950). *Acta paediat. (Uppsala)*, **39**, 453.
Suter, W. E., Schaefer, W. B., and Dubos, R. J. (1951). *Bact. Proc.*, **51**, 90.
Sweany, H. C. (1956). *Dis. Chest*, **29**, 346.
Thrap-Meyer, H. (1954). *Acta tuberc. scand.*, **29**, 173. See also p. 180 and p. 188.
Torres, F. E., Myers, J. A., and Harrington, F. E. (1944). *J. Lancet*, **64**, 67.
Tuberculosis Vaccines Clinical Trials Committee, M.R.C. (1956). *Brit. med. J.*, **1**, 413.
United States Department of Agriculture (1959). *Cooperative State-Federal Tuberculosis Eradication Program. Statistical Tables, Fiscal Year 1958*. Animal Disease Eradication Division, Agricultural Research Service, Washington, D.C.
Vorwald, A. J. (1932). *Amer. Rev. Tuberc.*, **25**, 74.
—— Dworski, M., Pratt, P. C., and Delahant, A. B. (1954). Ibid., **69**, 766.
Wallgren, A. (1955). *Acta paediat. (Uppsala)*, **44**, 237.

LONG-TERM EFFECTIVENESS OF B.C.G. VACCINATION OF INFANTS IN CLOSE CONTACT WITH INFECTIOUS TUBERCULOSIS

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It has been demonstrated many times that B.C.G. vaccination can prevent tuberculosis. For example, Aronson *et al.* (1958) vaccinated 1,557 American Indian children 20 years ago and left 1,457 as controls. The incidence of tuberculosis in that community was high at the time these vaccinations were done. Twenty years later they were able to account for over 99% of both groups, and found that 104 (6.7%) of the vaccinated subjects had died. Tuberculosis was responsible for 0.8% of the deaths. Of the controls, 150 (10.4%) died, including 4.7% from tuberculosis. The excess of deaths in the control group was entirely due to deaths from tuberculosis. Hyge (1947) observed an epidemic of tuberculosis in a school in Denmark. Of 94 tuberculin-negative children who were exposed to an infectious school teacher, 41 developed tuberculosis; whereas of 106 B.C.G.-vaccinated children who were exposed to the same infection, only two developed the disease. The Medical Research Council (1956) conducted a large-scale controlled trial on adolescent boys and girls. It was found that the annual incidence of tuberculosis in the initially tuberculin-negative unvaccinated group was 1.94 per 1,000, whereas in the B.C.G.-vaccinated group it was only 0.37 per 1,000.

Present Investigation

In this country there have been no reports so far about the long-term effectiveness of B.C.G. vaccination in contacts. We have therefore decided to review the results of B.C.G. vaccination in all the 267 children who attended our contact clinic, and who were under the age of 2 years when they were vaccinated with B.C.G. between October, 1949, and October, 1952. All of those who had been in contact with an active case of tuberculosis were segregated for six weeks after the initial negative tuberculin test. They were then retested and when a second negative result had been obtained were immediately vaccinated with 0.1 ml. of the liquid Danish B.C.G., given intradermally over the left deltoid. A further period of segregation followed for six weeks, or for a longer period if by then tuberculin conversion had not taken place. In the case of newborn infants in potential contact with a case of tuberculosis the initial tuberculin tests were omitted. These were vaccinated at birth with 0.2 ml. of B.C.G. and segregated until tuberculin conversion was demonstrated. After tuberculin conversion all were allowed to return home, irrespective of the condition of the index case.

The children were then seen at approximately annual intervals, or more often if required At the end of the third year and annually thereafter the tuberculin tests

were repeated and radiographs of the chest were taken. A number of children left the district and were transferred to other chest clinics for the parents' convenience, and we have lost trace of others. For the purpose of this survey we made a special effort to trace and examine as many of these as possible.

Results

Between the summer of 1957 and the spring of 1958 we were able to trace 261 of the 267 children who had been vaccinated five or more years earlier. As Table I shows, three had died of non-tuberculous illnesses (consisting of leukaemia in two and paralytic poliomyelitis in one). Ten others were alive and well

TABLE I.—*Follow-up of Contacts Who Had Been Vaccinated with B.C.G. During Infancy Between October, 1949, and October, 1952*

	No.	%
Total vaccinated	267	100
Died of tuberculosis	0	0
,, ,, other causes	3	1·1
Untraced: Emigrated	4	1·5
Untraced: No information	2	0·7
Known alive and well; refused to be examined	10	3·7
Seen and examined in 1957–8	248	92·9

and were seen by our health visitors; they were going to school, but their parents refused to attend with them for examination and did not agree to tuberculin-testing. The remaining 248 (92.9%) were seen, examined, and tuberculin-tested, and radiographs of the chest were obtained in 235 of them. Of the six children untraced, four were known to have emigrated, and we have no information about the remaining two, five years after their vaccination.

Tuberculin Tests.—The method of tuberculin-testing the 248 who were followed up was largely guided by convenience (Table II). In the large majority the initial test was the tuberculin jelly test, which was applied by the health visitor in the child's home and the results of

TABLE II.—*Results of 248 Tuberculin Tests Performed in 1957–8 on Children Vaccinated in 1949–52*

	No.		%
Total positive	243	..	98·0
Jelly	128		
Mantoux (10 or 100 T.U.)	36		
Heaf	79		
Total negative	4*	..	1·6
Mantoux (10 or 100 T.U.)	3		
Heaf	1		
Not read	1	..	0·4

* Revaccinated.

which were read by one of us at the contact clinic. If the result was negative, intradermal or percutaneous tests were used. The latter were the primary tests on those who attended without having had a tuberculin jelly test at home. Of the 248 tested, 243 (98%) were tuberculin-positive, four were tuberculin-negative, and one failed to attend for reading of the test. The four negative reactors were revaccinated, and they responded with a typical primary B.C.G. lesion like tuberculin-negative children.

Radiographs of Chest.—These were obtained in 235 of the 248 patients followed up for five years, and were normal in 232 (Table III). There were only 3 (1.2%) children in whom tuberculous lesions were found and

TABLE III.—*Results of 235* Radiographs of Chest of Children Seen in 1957–8*

Result	No.	%
Normal	232	98·8
Calcified lesions	3	1·2

* In 13 cases radiographs were not taken.

which led to pulmonary and hilar calcification. One of these children never had any symptoms suggestive of tuberculosis or of respiratory disease, and his pulmonary lesion was a minute calcified focus. The other two were subject to recurrent cough. Clinically their infection was mild, and neither patient required anti-tuberculous chemotherapy. Their case histories are given in full.

Case 1

The patient was first seen at the age of 4 months as a contact of her grandfather, who had chronic old-standing pulmonary tuberculosis and was being admitted to a sanatorium the next day. He was sputum-positive. The infant was well and tuberculin-negative. She remained tuberculin-negative to 100 T.U. of old tuberculin (Mantoux) up to September, 1952, eight weeks after separation from contact. She was then vaccinated with B.C.G. A tuberculin-jelly test six weeks later was positive. The B.C.G. produced the usual small lesion. An ulcer had been present at the site of the vaccination, but it had healed by the time she was seen for a conversion test. There had been no further contact with the grandfather, who remained in the sanatorium until this time. Later he was discharged from the sanatorium and frequent contact was resumed. The child remained in good health up to one year after vaccination. She did not keep subsequent appointments, but was seen eventually four and a half and again five and a half years after vaccination. She was said to have been quite well, but on more detailed inquiry it appeared that she was subject to recurrent cough, causing much loss of time from school. On physical examination she was in excellent condition and had no abnormal signs. She weighed 44 lb. (20 kg.) at the age of 6 years. The tuberculin-jelly test was positive. Radiographs of her chest showed a well-calcified primary complex in her left upper lobe, with a segmental collapse (Fig. 1).

Meanwhile her grandfather had died of tuberculosis in 1955. There were no other cases of known tuberculosis in the family.

Comment.—It is possible that this infant contracted tuberculosis when contact was resumed with her infectious grandfather, in spite of a successful conversion following B.C.G. vaccination. Alternatively,

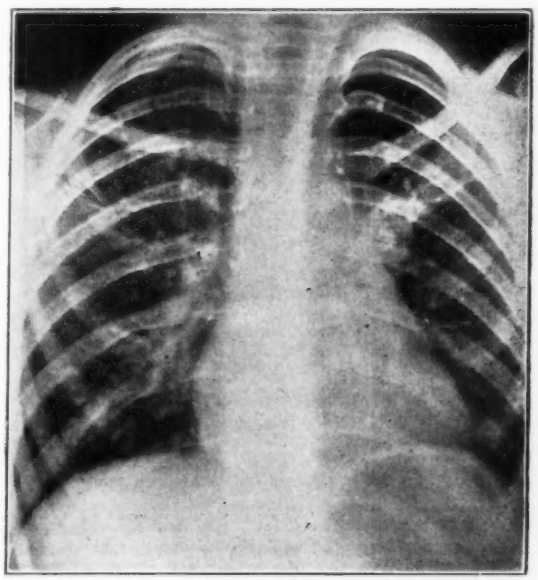

FIG. 1.—Case 1. Partial collapse of left upper lobe with calcified complex.

she might have been infected by an unknown person, possibly before the vaccination took effect.

Case 2

This child was 18 months old when she was first seen on account of contact with her tuberculous mother, who was admitted to a sanatorium the same day. The mother had had a cough for three months, and five weeks before her admission to the sanatorium was found to have pulmonary tuberculosis. Her children were then taken to the paternal grandmother. The mother had not seen this infant for three weeks prior to the baby's first visit to the clinic. The baby was then well and tuberculin-negative. Six weeks later she was negative to 100 T.U. of old tuberculin and was vaccinated with B.C.G. A further 10 weeks later she was positive to tuberculin jelly, and her B.C.G. lesion was a typical 12-mm. papule with a central crust on it. The mother was kept in hospital until conversion had taken place, and was then discharged home and contact was resumed.

The child remained well, but when seen at a routine visit three and a half years after vaccination she had a cough associated with rales in her chest. A radiograph of her chest then showed partial collapse of her left lower lobe as well as a round lesion in the right upper lobe and enlargement of the right hilum (Fig. 2). This lesion was consistent with a recent primary tuberculous infection. She was given a course of sulphadimidine, but, although her cough improved during the next two weeks, there was no significant change either in the physical signs or in the *x*-ray appearances. She was admitted for investigation, and for more energetic treatment with intramuscular penicillin, postural drainage, and physiotherapy. The physical signs disappeared, but her radiological lesions persisted. During her stay in hospital three consecutive gastric washings were cultured for tubercle bacilli and were inoculated into guinea-pigs, all with negative results.

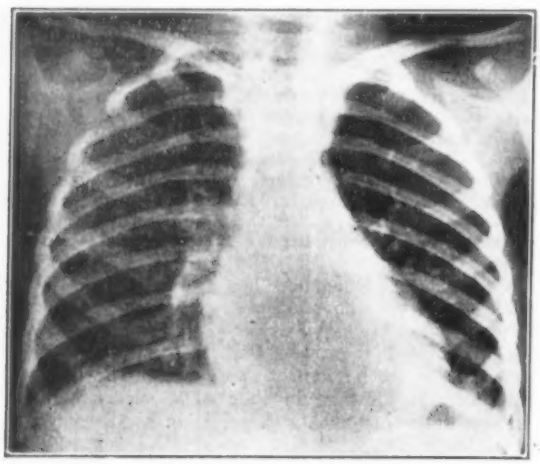

FIG. 2.—Case 2. Partial collapse of left lower lobe, a round lesion in right upper lobe, and enlargement of right hilum.

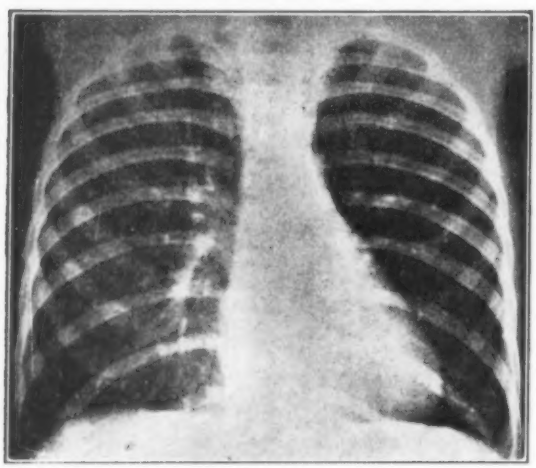

FIG. 3.—Case 2. Calcified shadow in right upper lobe, scattered calcifications in lower half of left lung, and partial collapse of left lower lobe.

After this admission the family removed from the district, and the child was not seen again until three years later, when they returned to Sheffield. The child had had no illnesses meanwhile, but her cough persisted. It now became known that her paternal grandmother, who looked after her while the mother was in the sanatorium, also had pulmonary tuberculosis. This was not known at the time she was in charge of the baby.

The child now had persistent rales over her left lower lobe, and the radiograph of her chest showed a calcified shadow in the right upper lobe, scattered calcifications in the lower half of the left lung, and partial collapse of the left lower lobe (Fig. 3). At this time the mother became ill again, and was readmitted to the sanatorium with tuberculous laryngitis and a cavity in her right lung.

Comment.—It is probable that this child was infected by her grandmother during the pre-allergic phase. It is possible, however, that she was infected either by her mother or by the grandmother after tuberculin conversion following the B.C.G. vaccination.

The Index Cases

In order to assess the protective value of B.C.G. in these children it is clearly necessary to know the nature of the contact with tuberculous persons. All of these were household contacts (Table IV). The parents were the "index" cases in 116 (47%), the grandparents in 31 (12.4%), and other persons in 101 (40.6%). The fact that more than half the index cases were not members of their immediate family reflects the overcrowding and poor living conditions of these families during the period under review.

TABLE IV.—*Index Cases and Their Subsequent Progress*

	No.	%
Principal potential source of infection:		
Mother	65	26·2
Father	51	20·8
Grandparents	31	12·4
Other relatives of household contacts	101	40·6
Condition at time of vaccination:		
"Active"	202	81·4
"Inactive"	46	18·6
Condition at time of this survey:		
Died of tuberculosis	39	15·7
Still active tuberculosis	28	11·3
Quiescent	170	68·5
Not known	11	4·4

More than four-fifths of the index cases were considered to have active tuberculosis at the time the children came under our care. The remainder were "inactive" in the sense that they had negative sputum. We know from past experience, however, that "inactive" cases may well cause fatal infection in children (Briggs, Illingworth, and Lorber, 1955). During the period of observation 39 (15.7%) of the index cases ended in death from their tuberculosis after variable periods of fluctuating fortune; 28 (11.3%) had either been persistently active or were considered to be in the

active stage again at the time of this review; and 170 (68.5%) were no longer active. We have no information about the last 11.

Conclusions and Summary

As there was enough evidence available by 1949 that B.C.G. was of value in the prevention of tuberculosis, it would have been ethically indefensible to withhold B.C.G. vaccination from any of our contact babies and so study comparable series of unvaccinated controls. Consequently, there is no absolute evidence that B.C.G. vaccination prevented tuberculosis in any. Nevertheless, the fact that from such a particularly unfavourably situated group of infants none died of tuberculosis, and only two developed symptoms which could possibly be attributed to tuberculous infection, suggests that the vaccinations were of value. It is more definite and satisfactory to record the prolonged effectiveness of the vaccination as judged by the persistence of the positive tuberculin reaction in 98% of the cases for five years or more.

267 children aged 2 years or less who were in close household contact with cases of tuberculosis and who remained tuberculin negative six weeks after segregation from contact were vaccinated with B.C.G. between October, 1949, and October, 1952. Of these, 261 were traced five years or more after vaccination. There were no deaths from tuberculosis; only two had minor clinical symptoms associated with tuberculous lung lesions which healed by calcification, and one other had a calcified lung lesion. There were only four who reverted and became tuberculin negative. In contrast, of the "index" cases 39 (15.7%) died of their tuberculosis and 28 (11.3%) still had active disease at the time of this review.

As there were no comparable controls it cannot be shown conclusively that B.C.G. vaccination prevented tuberculosis in this group of infants. Nevertheless the results are highly suggestive that this, in fact, was the case.

It is a pleasure to acknowledge and thank the help given by the chest physicians of Sheffield and many other areas; Dr. Llywellyn Roberts, the Medical Officer of Health of Sheffield, and his health visitors; and Dr. Marion C. Taylor, principal school medical officer of Sheffield, without whose help it would have been impossible to secure such a full follow-up; Professor R. S. Illingworth for his criticism; and the Tuberculosis Research Fund of the University of Sheffield for its grant to one of us (P. C. M.).

REFERENCES

Aronson, J. D., Aronson, C. F., and Taylor, H. C. (1958). *A.M.A. Arch. intern. Med.*, **101**, 881.

Briggs, B., Illingworth, R. S., and Lorber, J. (1955). *Lancet*, **1**, 263.

Hyge, T. V. (1947). *Acta tuberc. scand.*, **21**, 1.

Medical Research Council (1956). *Brit. med. J.*, **1**, 413.

The second edition of Colonel Sir R. N. Chopra's *Indigenous Drugs of India* has been largely rewritten by the original author in collaboration with I. C. Chopra, K. L. Handa, and L. D. Kapur. In its preparation account has been taken of the considerable accumulation of relevant literature since the appearance of the first edition in 1933. This is a very useful reference book, carefully documented and fully indexed. It is published by Dhur and Sons Ltd., 15, Bankim Chatterjee Street, Calcutta, 12 (pp. 816+xxxii; 1958. £5 5s.).

"B.C.G. SARCOIDOSIS"

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Since the earliest major contributions on sarcoidosis were made (Hutchinson, 1875–8; Besnier, 1889; Boeck, 1899, 1905; Schaumann, 1914; Jüngling, 1919) the aetiology has been much debated. Hutchinson (1898), in his study of the disease, thought the cause "may not improbably be a tuberculous affection and one of the lupus family." A large school of thought believes sarcoidosis to be a group of granulomatous diseases of known distinct aetiology—for example, tuberculosis, histoplasmosis, brucellosis, berylliosis—or to be idiopathic. Scadding (1950, 1956b) recommended the use of the terms "tuberculous sarcoid," "histoplasma sarcoid," "beryllium sarcoid," etc., whilst idiopathic cases belong to the tuberculous group passing through an unusual phase of tuberculosis. In latter years cases of sarcoidosis occurring in patients previously given B.C.G. vaccination have been recorded in the literature (Larsen, 1950; Löfgren and Lundbäck, 1952; Törnell, 1954; Pfisterer *et al.*, 1954; Ganguin, 1956; Birkhäuser, 1957; Fried and Genz, 1958). The term "B.C.G. sarcoidosis" is being applied to these cases. We record here a further case of histologically proved sarcoidosis occurring in a girl given B.C.G. vaccination seven years previously.

Case Report

In December, 1950, when the patient was 14 years old, she was vaccinated with Danish B.C.G. as a Mantoux-negative school-leaver. She was subsequently followed up under the Medical Research Council Tuberculosis Vaccines Clinical Trial by skin-sensitivity testing and chest *x*-ray examinations (see Table).

Results of Follow-up

Date	Skin Test (Same Batch of Old Tuberculin was used throughout except on 2/9/57 and 1/9/58)	Chest *X*-Ray Examination
1/12/50	Negative 1/100	Normal
7/12/50	*B.C.G. vaccination*	
26/2/51	Positive 1/3,000 (10 mm.)	,,
8/7/52	—	,,
18/11/53	Positive 1/3,000 (7 mm.)	,,
16/2/55	Negative 1/3,000	
	Positive 1/100 (12 mm.)	,,
15/5/56	Positive 1/3,000 (14 mm.)	,,
23/7/57	Negative 1/3,000	Reticular mottling right upper and mid-zones and left upper zone
2/9/57	Negative 1/1,000	Reticular mottling of whole of right lung and left upper and mid-zones
12/9/57	,, 1/100	
1/9/58	Heaf test positive	Normal

In July, 1957, her Mantoux reaction (1/3,000) had become negative, and reticular mottling had appeared in the right upper and mid-zones and left upper zone of her chest *x*-ray picture. In September she was admitted to Plaistow Hospital Chest Unit under the care of one of us (P. E.).

The patient was asymptomatic. On examination small cervical and scalene glands were palpable and the liver edge was felt one fingerbreadth below the right costal margin. The spleen was just felt on inspiration. The results of further investigations were: haemoglobin, 12.6 g./100 ml.

(87%); W.B.C., from 5,000 to 9,000/c.mm., with a normal differential; E.S.R., 21 mm./hour (Westergren); total serum protein, 6.9 g./100 ml. (albumin 4.4 g., globulin 2.5 g.); serum protein electrophoretic pattern normal; serum calcium, 5 mEq/l.; inorganic phosphorus, 3.2 mEq/l.; serum bilirubin, 0.4 mg./100 ml.; alkaline phosphatase, 3.3 units; thymol turbidity, 4.5 units; zinc sulphate, 5.5 units; laryngeal swabs and gastric and tracheal lavages negative for acid-fast bacilli; *x*-ray film of the hands normal. The chest *x*-ray film showed reticular mottling involving the whole of the right lung field and the left upper and mid-zones (Fig. 1). A liver biopsy showed florid changes compatible with sarcoidosis; there were multiple granulomata exhibiting giant-cell formation, but no caseation was seen nor were acid-fast bacilli demonstrated. The Kveim test was negative, using two different potent antigens.

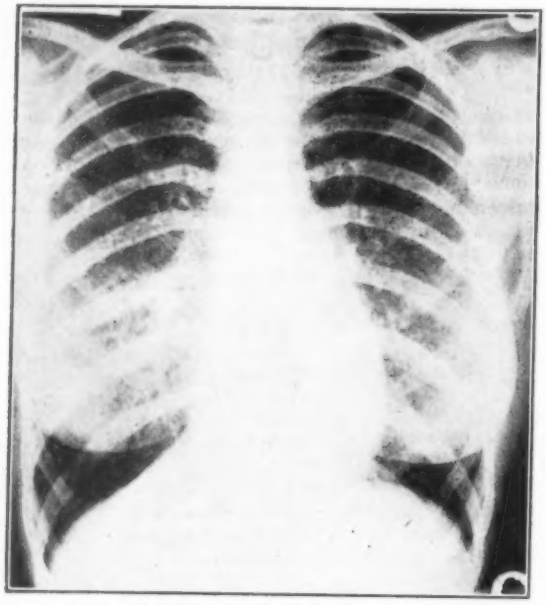

FIG. 1.—*X*-ray film showing reticular mottling involving almost all of right lung field and left upper and mid-zones.

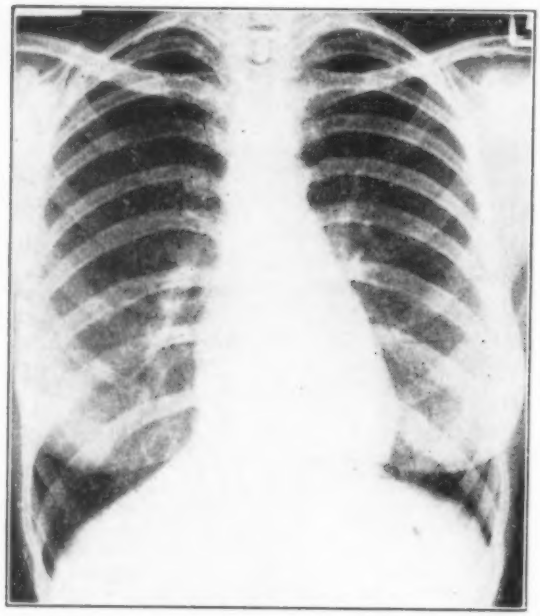

FIG. 2.—Twelve months later. *X*-ray film showing complete resolution of lung reticulation.

The patient was given no active treatment, and after her discharge from hospital in October, 1957, she returned to work. In December she continued to be asymptomatic, no abnormalities could be elicited clinically, and the chest *x*-ray film showed obvious evidence of resolution. Radiological improvement continued, and by September, 1958, the chest *x*-ray film was within normal limits. At that time the W.B.C. was 4,500/c.mm., with a normal differential; E.S.R., 6 mm./hour; total serum protein, 7.9 g./100 ml. (albumin 4.7 g., globulin 3.2 g.); serum protein electrophoretic pattern normal; serum calcium, 5 mEq/l.; and the Heaf tuberculin test was positive. Her chest *x*-ray picture (Fig. 2) has continued to be normal.

Discussion

Berg (1940) first described a regional lymphadenitis after B.C.G. vaccination, presenting the histological picture of sarcoidosis. Since then, as already mentioned, several references to sarcoidosis occurring in B.C.G.-vaccinated subjects have appeared in the world literature. A proportion of these cases fulfilled the histological criteria; in others the diagnosis was made on radiological and/or clinical grounds. Ganguin (1956) reported two vaccinated siblings exposed to tuberculosis, one of whom developed sarcoidosis, the other's illness being interpreted as atypical tuberculosis. The negative Kveim test in our case is still in keeping with the diagnosis. In a series of 110 Kveim tests the investigation has proved positive in 75% of patients with sarcoidosis (James, 1956). In a world survey of 560 patients with biopsy-confirmed sarcoidosis Siltzbach (1957) found that the positive Kveim reaction ranged from 65 to 92%.

The onset in most cases was within three years of inoculation. Fried and Genz (1958) have added a further 12 cases (six verified histologically), the ages of the patients at the time of vaccination being between 6 and 10 and at the onset of sarcoidosis between 12 and 21. The time interval after inoculation varied from 18 to 90 months, the average being five years. In our case the interval was seven years.

In the cases of Löfgren and Lundbäck (1952) spontaneous remissions often occurred, but in those of Fried and Genz (1958) only one is recorded. Five of the last-named authors' cases responded partially to antibiotic and hormonal therapy, but some of these might have improved had treatment not been given. In our case the recovery was spontaneous.

Patients with sarcoidosis are unable to develop and maintain skin sensitivity to tuberculin after B.C.G. vaccination (Israel *et al.*, 1950; Forgacs *et al.*, 1957). Many patients with sarcoidosis are known to have been tuberculin-positive prior to the onset of sarcoidosis. The sensitivity wanes and disappears when clinical symptoms of sarcoidosis appear, and when sarcoidosis subsides the sensitivity to tuberculin may return (Nitter, 1953). In some cases the previous history may reveal failure to convert to positive after vaccination (James, 1958). In the cases of Fried and Genz (1958) and in 17 of the 25 cases referred to by Löfgren and Lundbäck (1952) the tuberculin allergy became negative or distinctly weaker. Our patient followed the usual course; she developed positive skin sensitivity after vaccination, which was not maintained during the sarcoidosis, but reverted to positive when she recovered.

Mather *et al.* (1955) and Scadding (1956a) believe there is often a direct aetiological relationship between tuberculosis and sarcoidosis. Those who support the tuberculous aetiology would regard sarcoidosis as an example of tuberculous infection in which there is a high resistance and immunity, but in which immunological response has been associated with marked granulomatous formation (Robb-Smith, 1956). None the less, this combination in the same patient is not often found (Cowdell, 1954). In sarcoidosis the patient appears to have an enhanced capacity to destroy tubercle bacilli in the tissues, which accounts for the inability to identify them in sarcoid follicles. This cannot apply to acid-fast bacilli as a whole, as B.C.G. organisms remain alive at vaccination sites for as long a period in patients with sarcoidosis as in normal susceptible controls (Rostenberg *et al.*, 1953 ; Forgacs *et al.*, 1957).

It is possible that sarcoidosis and B.C.G. vaccination are coincidental (Törnell, 1954 ; James, 1958). The incidence of sarcoidosis as compared with tuberculosis is greater in vaccinated than in unvaccinated groups of patients, and the discrepancy is too great to be accidental (Fried and Genz, 1958). The incidence of post-B.C.G. sarcoidosis is higher than the normal morbidity rate for sarcoidosis in Switzerland (Birkhäuser, 1957). It is unlikely that the B.C.G. vaccination precipitates sarcoidosis in view of the long time interval between vaccination and the onset of sarcoidosis in our own and other writers' cases, although in leprosy there can be an interval of up to 20 years between contact and the development of granulomatous formation (Muir, 1948). Löfgren (1953) thinks vaccination may provoke sarcoidosis in patients when the disease is latent. It may well be that without B.C.G. vaccination these cases would normally have developed tuberculosis and that the vaccination protects and modifies the case to one of sarcoidosis. In this country more cases may appear as more school-leavers are vaccinated and followed up for several years. In children under 15 years of age only 113 cases of sarcoidosis had been recorded in a world survey of the literature (McGovern and Merritt, 1956).

Summary

A histologically proved case of sarcoidosis occurred in a girl given B.C.G. vaccination seven years previously. She recovered spontaneously, and the tuberculin sensitivity, which became negative during her illness, reverted to positive. The literature on the occurrence of sarcoidosis in B.C.G. vaccinated cases is reviewed. It is suggested that had she not been vaccinated she might have developed tuberculosis instead of sarcoidosis. The time interval was too long for vaccination to be regarded as the cause of the sarcoidosis.

We thank Dr. T. M. Pollock for kindly referring this case to us, and Dr. Sheila Sherlock and Dr. Geraint James for their help with the liver biopsy and Kveim tests respectively.

REFERENCES

Berg, S. (1940). *Acta med. scand.*, **103**, 8. Quoted by E. Sommer, *Schweiz. Z. Tuberk.*, **12**, 163.
Besnier, E. (1889). *Ann. Derm. Syph. (Paris)*, **10**, 333.
Birkhäuser, H. (1957). *Schweiz. med. Wschr.*, **87**, 1434.
Boeck, C. (1899). *J. cutan. Dis.*, **17**, 543.
—— (1905). *Arch. Derm. Syph. (Wien)*, **73**, 71.
Cowdell, R. H. (1954). *Quart. J. Med.*, **23**, 29.
Forgacs, P., McDonald, C. K., and Skelton, M. O. (1957). *Lancet*, **1**, 188.
Fried, K. H., and Genz, H. (1958). *Tuberk-Arzt.*, **12**, 558.
Ganguin, H. G. (1956). *Allergie u. Asthma*, **2**, 88.
Hutchinson, J. (1875–8). *Illustrations of Clinical Surgery*, **1**, 39. London.
—— (1898). *Arch. Surg. (Lond.)*, **9**, 307.
Israel, H. L., Sones, M., Stein, S. C., and Aronson, J. D. (1950). *Amer. Rev. Tuberc.*, **62**, 408.
James, D. G. (1956). *Brit. med. J.*, **2**, 900.
—— (1958). *Postgrad. med. J.*, **34**, 240.
Jüngling, O. (1919). *Fortschr. Röntgenstr.*, **27**, 375.
Larsen, A. K. (1950). *Nord. Med.*, **43**, 170.
Löfgren, S. (1953). Quoted by Fried and Genz (1958).
—— and Lundbäck, H. (1952). *Acta med. scand.*, **142**, 265.
McGovern, J. P., and Merritt, D. H. (1956). *Advanc. Pediat.*, **8**, 97.
Mather, G., Dawson, J., and Hoyle, C. (1955). *Quart. J. Med.*, **24**, 331.
Muir, E. (1948). *Manual of Leprosy*, p. 10. Livingstone, Edinburgh.
Nitter, L. (1953). *Acta radiol. (Stockh.)*, Suppl. 105.
Pfisterer, R., Wespi, H., and Herzog, H. (1954). *Helv. med. Acta*, **21**, 439.
Robb-Smith, A. H. T. (1956). *Proc. roy. Soc. Med.*, **49**, 1041.
Rostenberg, A., Szymanski, F. J., Brebis, G. J., Haeberlin, J. B., and Senear, F. E. (1953). *A.M.A. Arch. Derm. Syph.*, **67**, 306.
Scadding, J. G. (1950). *Brit. med. J.*, **1**, 745.
—— (1956a). *Proc. roy. Soc. Med.*, **49**, 799.
—— (1956b). *Tubercle (Lond.)*, **37**, 371.
Schaumann, J. (1914). *Sur le lupus pernio*. Paris.
Siltzbach, L. E. (1957). *Amer. J. Med.*, **22**, 841.
Törnell, E. (1954). *Nord. Med.*, **52**, 996.

CONTROLLED HYPOTHERMIA IN INFANTS AND CHILDREN

BY

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The use of hypothermia now occupies a definite though restricted place in medicine. When we know more concerning oxygen transfer to the body cells, and its utilization by them during hypothermia, many of the present restrictions governing the use of lowered body temperatures may be removed, and the indications for its use may be extended considerably.

In cardiac surgery in children, when hypothermia is utilized, various technical requirements are desirable, the essential elements of which are :

1. A central body temperature which can be maintained accurately at any desired level, usually 30° C. This is estimated by the temperature recorded in the lower third of the oesophagus. Cooper and Kenyon have shown this to be a fairly accurate assessment of the central blood stream temperature during surface cooling, and we have also found that this temperature corresponds very closely to the temperature of the cerebral cortex.

2. A reasonable rate of fall in body temperature. This should be rapid enough to avoid the necessity for any extension of the normal operating-time.

3. Means whereby the body temperature may conveniently be raised or lowered while surgery is in progress.

4. Restoration of the body temperature to normal, as soon as possible after the completion of the operation, with minimal handling of the patient.

5. Accurate control of the rate of change of body temperature and facilities to stabilize it rapidly at any desired level, thus preventing any "overswing."

*Aided by a grant from the Royal Australasian College of Physicians.

6. The avoidance of additional major surgery solely for the purpose of producing cooling.

The use of blood-stream "extracorporeal" cooling as utilized by Delorme (1952), Ross (1954), and Lucas (1956) fulfils most of these requirements, but it has various technical, mechanical, and physiological disadvantages, which are discussed later.

Present methods of surface cooling, with or without the use of long-acting drugs (Bigelow *et al.*, 1950; Swan *et al.*, 1953; Lewis and Taufic, 1953; Dundee *et al.*, 1953; Bailey *et al.*, 1954; Ripstein *et al.*, 1954), do not fulfil these requirements. It is difficult to control the rate of cooling, and it is impossible to assess or to control the duration and degree of "overswing." There is also very little in the way of cooling or rewarming that can be done whilst the surgeon is at work.

The use of intragastric cooling (Khalil, 1957) is slow and not a practical proposition in association with surgery.

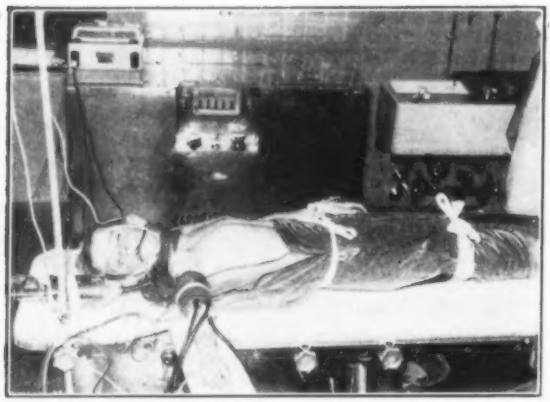

FIG. 1.—The patient is shown on the operating table with "polythene"-covered rubber blankets tied in close contact with the body. In the background is the "hypothermia machine," and on its top left-hand corner is the electrical thermometer.

The method presented here of inducing hypothermia and rewarming is by body-surface action. The skin of the patient is in close contact with rubber blankets containing a continuous capillary through which iced, hot, or tepid water is pumped and recirculated. The machine used to supply and pump the water is shown in Fig. 1.

Equipment

*Hypothermia Machine.**—This contains three copper tanks, one of which contains 6 gallons (27.3 litres) of hot water thermostatically controlled at 40–42° C.; another contains 5 gallons (22.7 litres) of water at a temperature of 25–28° C.; and the final tank has 2½–3 gallons (11.4–13.6 litres) of water at 2–3° C. Outflow and inflow connexions for five blankets are housed below a central control panel, which regulates the rate of flow through each blanket, also the contents of the blankets, hot, tepid, or ice-cold water. Automatic valves ensure non-mixing between tanks when the water circulating in the blankets is changed from one tank to another. Hence it is possible to circulate water from any tank through any blanket at whatever rate is required. The temperature gradient between the outflow and inflow connexions on the machine when circulating iced water at the usual flow rate is less than 1.5° C. The total amount of ice cubes used averages about 40 lb. (18 kg.) over a period of three to four hours, which is the average time taken on such cases. The machine is portable and readily moved to a satisfactory position in the operating theatre. The length of tubing from the machine to the blankets will determine its distance from the patient; about 6 feet (1.8 metres) has been found a convenient distance. All connexions are of a simple bayonet self-sealing type.

Blankets.†—These are made of rubber and contain a continuous capillary enabling water to be circulated throughout their entirety; this assures an even distribution of temperature all over the blanket. Three blankets measuring 18 by 40 in. (46 by 101 cm.), 12 by 32 in. (30 by 81 cm.), and 8 by 32 in. (20 by 81 cm.) have been found adequate for all cases, from small babies to children 13 years of age.

Temperature Recorder.—It is essential to have available facilities for accurately and quickly recording the body temperature, preferably in more than one situation. The recording apparatus should be situated conveniently close to the hypothermia machine, and well away from the patient so that no inconvenience will be caused to the surgeons or anaesthetists during the operation. The electric universal thermometer, type T.E. 3, manufactured by Elektrolaboratoriet, Copenhagen, has been found admirably suited to our requirements. Rectal and lower oesophageal leads are regularly employed, and a periodic check of the pharyngeal temperature may be made by the anaesthetist, using a mercury thermometer. In addition a needle applicator, with a thermojunction situated at the needle tip, has been used experimentally to measure the temperature in the cerebral cortex and the aorta during cooling, both of which closely correspond to the temperature in the lower third of the oesophagus.

Methods

The anaesthetized unclothed patient is placed on the operating table on a large rubber blanket. All leads are then connected—for example, rectal and oesophageal for temperature recording, intra-arterial "polythene" tubing for continuous blood pressure, subcutaneous needles for E.C.G. and the diathermy plate. It is considered essential to monitor the heart's action continuously, using a cathode-ray oscilloscope, whenever hypothermia is employed—in fact, this safeguard is used routinely for all cardiac surgical procedures in our unit. In all "open heart" procedures a continuous record of the intra-arterial blood pressure is also regarded as desirable.

The child is placed in position, supine or lateral, depending on the nature of the operation. A blanket is placed on top of the patient, covering the abdomen and legs, and a narrow blanket is placed between the legs and thighs. The blankets are then tied together, overlapping where necessary, but obtaining maximum contact with the skin. The only exposed parts of the body are the head, neck, arms, and that part of the thorax where the surgeon is to operate (Fig. 1).

A long piece of rubber tubing, ¼ in. (1.3 cm.) external diameter, is then coiled around the neck, fitting snugly but not too tightly, and making as many coils as possible in order to obtain maximum skin contact; this is usually

*Manufactured by Ebsray Pumps Pty. Ltd., Sydney.

†Manufactured by Dunlop Rubber, Australia, Ltd., Sydney.

three to four coils (Fig. 2). This tubing makes the fourth connexion with the machine, leaving one spare connexion.

Water at 2–4° C. is circulated through all the blankets and the neck coil. The rectal and oesophageal temperatures are recorded at regular intervals in graph

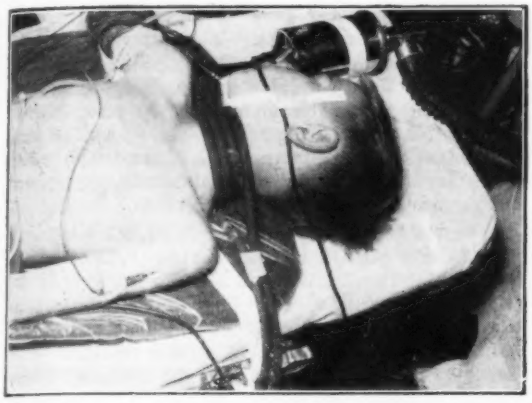

FIG. 2.—The neck coil is shown in position. The chest is exposed for bilateral thoracotomy.

form, and so long as no alterations are made to the rate of flow through the blankets or the temperature of the water contained therein, it is found that there is a linear rate of fall in the body temperature. The exact time can be predicted at which the body will cool to any desired temperature. As the body temperature falls and approaches the required level it is possible to circulate tepid or hot water through any or all of the circuits simply by turning the control knob, or any blanket can have its circulation stopped independently of the others. This allows great flexibility and ideal control.

As soon as the blankets have been connected and the patient has been positioned, the surgeon can scrub up and proceed with the operation; then, while the operation proceeds, the temperature is being lowered to the required degree, and when this point is reached it may be stabilized and held there. When desired, rewarming can be initiated by circulating hot water through the blankets, and by the time the operation is completed the temperature of the patient is invariably raised sufficiently to allow safe transport from the theatre. The child is then taken to a recovery ward together with the temperature-recording apparatus and placed in an oxygen tent. The temperature is regularly recorded at 10-minute intervals and active steps are taken to prevent any rise above 37° C.

Fifty patients have been subjected to this procedure, their ages ranging from 3½ months to 12 years. These cases have included the following conditions: atrial septal defect, pulmonary stenosis, aortic stenosis, aneurysm of the pulmonary artery, transposition of the great vessels, very severe tetralogy of Fallot, coarctation of the aorta, an unusual case of mitral stenosis in a girl of 7 years (this will be the subject of a special case report), and one case of persistent ductus arteriosus in a 6-months-old baby in severe heart failure. Recently all cases of coarctation of the aorta have been operated on under hypothermia because it is believed that the danger of a spinal artery thrombosis is lessened, and the slower heart rate greatly relaxes the aorta and makes it safer and easier to handle during its repair. In addition we have been impressed with the post-operative course of these patients, who require smaller and less frequent doses of analgesic and sedative drugs in the immediate post-operative period. They are obviously much less distressed by the procedure than similar cases operated on at normal temperatures. The decision to utilize hypothermia in the repair of coarctation of the aorta in children was made following the occurrence of paraplegia, fortunately incomplete, after the otherwise uncomplicated resection of a coarctation in a boy of 8 years in whom it was necessary temporarily to occlude an aberrant right subclavian artery arising just above the site of the coarctation.

Results

The method of hypothermia and rewarming described above has produced most gratifying results in all cases. An adequate rate of cooling was invariably maintained, a typical case being shown in Fig. 3. Rapid rates of cooling are not advised (Lucas, 1958), as it is considered that an excessive gradient between peripheral and central-blood-stream temperatures heightens the incidence of ventricular fibrillation (Lucas, 1955).

The use of a coil of rubber tubing around the neck, bringing the circulating water into close proximity with the large vessels in the neck, accentuates the rate of fall in temperature; the resulting change in gradient is illustrated in Fig. 4. The average rate of fall in temperature in the six cases before using neck cooling was 4.5° C. an hour, and after neck cooling was introduced the average fall in temperature was 5.5° C.

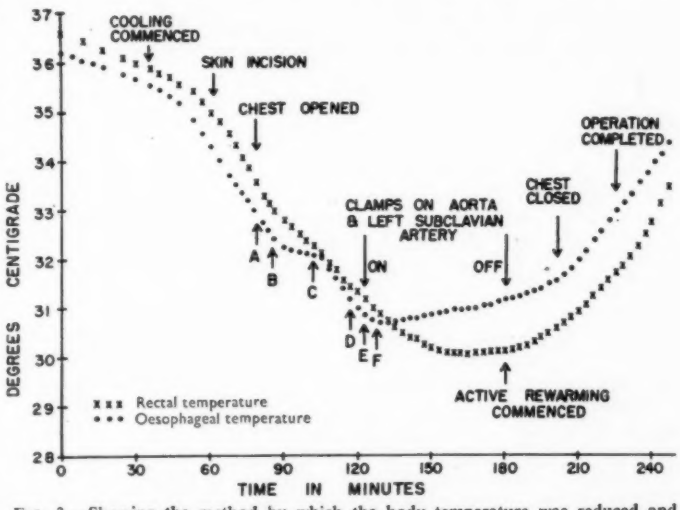

FIG. 3.—Showing the method by which the body temperature was reduced and restabilized at the lower temperature. A. Water circulation stopped. Iced water left in blankets. B. Hot water circulated for five minutes. C. Surgeon requested temperature to be lowered to 31° C. Iced-water circulation restarted. D. Water circulation stopped. Iced water left in blankets. E. Hot water circulated. F. Water circulation stopped. Hot water left in blankets and patient's temperature allowed to drift slowly upwards. Active rewarming begun as indicated by circulating hot water again.

an hour. In some of these latter cases it was necessary to exclude some of the circuits because the rate of cooling was unnecessarily rapid.

Infants and small children cooled at a more rapid rate than larger children owing to their greater surface area in proportion to their weight.

Other factors influenced the rate of cooling, such as a large shunt in the circulation or a coarctation with a poor blood supply to the lower half of the body, or an obese patient with a poor peripheral circulation. Such factors will retard the rate of cooling not only by this method but also by blood-stream (extracorporeal) methods. Even so, by the time the surgeon was ready to occlude the circulation the patient was always stabilized at the required temperature.

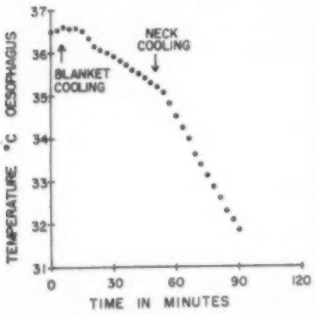

FIG. 4.—Illustrating the value of the neck coil in accelerating cooling. Blanket cooling only was used for the first 45 minutes, following which it was supplemented with the neck coil. The marked increase in the rate of cooling can be seen. Rewarming is also facilitated in a similar manner. Blanket cooling, 2.2° C. per hour; blanket plus neck cooling 5.25° C. per hour in this instance.

An appreciable variation has been found between body temperatures recorded at different sites, and this variation was often increased during cooling and rewarming of the body.

We consider it important that the body temperature recorded should approximate that of the cerebral cortex at the same moment. It was found that the temperature in the lower third of the oesophagus was always within 0.2° C. of the cerebral cortex temperature, both during cooling and rewarming and also while the temperature was stabilized. The pharyngeal or rectal temperatures were not nearly so satisfactory in this regard. The rectal temperature as shown in Fig. 3 reflected variations in cooling or rewarming very slowly.

In this case of coarctation of the aorta a temperature of 32° C. was asked for, but after opening the chest and inspecting the coarcted segment it was felt that the right subclavian artery might be aberrant and become involved in the clamps; hence it was decided to undertake the anastomosis at a temperature of 31° C. A close inspection of Fig. 3 will show the ease with which the body temperature was further reduced and restabilized at the lower temperature. Alterations in temperature were clearly shown in the oesophageal record, which we believe accurately reflects the central-blood-stream temperature, yet the rectal temperature recorded none of these changes; however, on close inspection it shows a slight change in the rate of fall in temperature some 10 to 15 minutes after this had already been demonstrated in the oesophageal lead. Also it will be seen how the rectal temperature gave a false impression of overswing, as the difference between rectal and oesophageal temperatures at the onset of rewarming was some 2° C. This crossing over of the rectal and oesophageal temperatures during cooling always occurred: they recrossed back to their original dispositions during rewarming. During stabilization the oesophageal temperature slowly rose for some 40 minutes while the rectal temperature was falling; however, it must be remembered that during this time no active steps were made to rewarm the patient, as the aim was to stabilize his oesophageal temperature at about 31° C. The average time taken to turn a patient's temperature from one of cooling to rewarming, or to stabilize it, was usually less than nine minutes.

From a comparison of the blood stream, cerebral cortex, and oesophageal temperature readings we believe that the recording of temperatures in the lower third of the oesophagus is reliable, and much more accurate than rectal or pharyngeal temperatures, and should be used in all cases of hypothermia. Delorme (1956) made a plea for conformity in taking the body temperature and suggested a mid-oesophageal recording.

Rewarming presented no difficulties, but temporary setbacks may occur if large amounts of cold blood are urgently transfused. All blood is now warmed to 35° C. prior to transfusion, and this problem has been eliminated. It is possible to rewarm the patient when the only effective circulation is cardiac massage. This was done on one occasion, and as the temperature rose the ventricular fibrillation present spontaneously reverted to sinus rhythm and the patient made an uneventful recovery.

No cardiac irregularities have occurred in this series that could possibly be attributed to the use of hypothermia.

The patients were rewarmed to at least 33° C. before removing the blankets, and were then taken from the operating theatre to a warmed bed. At this stage the rectal temperature, being within a degree of the oesophageal, was used to monitor the patient's temperature for the next 24 hours.

It was not necessary to rewarm patients actively over 33° C., as they always continued to rewarm at a steady rate without the aid of the blankets. Graphs were made of the temperature by the nursing staff, together with pulse and respiratory rates when in the recovery ward, and, if the temperature was not levelling off at or below 37° C., active measures were carried out, such as removal of all coverings, tepid sponging, reducing the temperature in the oxygen tent, or even placing ice-packs around the patient in order to achieve a normal stable body temperature.

It is important that the nursing staff should be familiar with these facts and thoroughly conversant with the procedure necessary to prevent hyperpyrexia developing.

Discussion

The body temperature of children undergoing cardiac surgery has been controlled with great satisfaction and safety since using this method of surface cooling with the machine circulating water through special rubber blankets.

Previously we had been accustomed to immersing children in a cold-water bath, drying them on removal, and placing them on an electric blanket that could be warmed. However, we were never satisfied, chiefly because we did not have adequate control. It was impossible to forecast the amount of overswing: the smaller the child the more difficult this became, and rewarming was difficult as the electric blanket was not adequate to perform this task. Further, the practice of

immersing a child with altered haemodynamics in a hot bath immediately after a long and sometimes difficult thoracotomy is not wise. There was also the question of delay and mess in the theatre prior to operation, extra handling of the patient, and extra movement of the attendants, such factors being apt to increase the risks of infection, prolong the duration of anaesthesia, and disturb the normal theatre routine.

The use of extracorporeal blood-stream cooling (Ross, 1954, 1956 ; Brock, 1956) must be restricted to patients undergoing bilateral or right thoracotomy. The blood is subject to the effects of pumping and also to very cold temperatures in the plastic tubing coil ; further, this tubing passes into the actively contracting heart, where it may remain for several hours, including the time when the circulation is occluded and the surgeon is repairing cardiac defects. This must represent a certain hazard, and is a major surgical procedure in itself. Also it introduces the possibility of trauma to the heart or great vessels, and might possibly distract the surgeon or interfere with his movements. The tubing can, of course, be disconnected and then reinserted for rewarming purposes, but this means extra handling of an overworked and irritable myocardium. In addition, there must be some risk of haemolysis or thrombosis of the blood in the extracorporeal circuit.

There are also mechanical problems such as flaws in the tubing, kinking during the pumping, inadequate venous return, and so on, any one of which could be serious if it occurred. Rewarming must be initiated and reach a certain stage before the heart can be closed and the operation completed ; this adds further to the delay, exposure, and handling of the heart.

In general it will be found that in our method the rate of cooling and rewarming is a little slower than the blood-stream cooling recommended and described by Ross (1954, 1956) and Brock (1956).

The advantages claimed for the method described are as follows: (1) There is no overall delay, since the operation can be started as soon as cooling has been initiated. (2) The procedure is extremely effective and controllable. Cooling and rewarming are achieved at a satisfactory rate, so that the desired temperature is reached by the time the surgeon requires it and adequate rewarming has been established by the time the operation has been completed. (3) No additional surgery is necessary to effect cooling, and it can be employed for any operative procedure for which it would seem to be indicated without necessarily opening the right chest or the pericardium. (4) It is not necessary to begin cooling prior to opening the chest, a decision for or against hypothermia being made after direct inspection of the lesion, if desired. (5) Rewarming is effective while the chest is open, and can be achieved whilst the circulation is maintained with cardiac massage, if necessary. (6) The procedure is simple, clean, and aesthetic, and there is minimal interference with the normal aseptic ritual in the operating theatre.

Our thanks are due to Dunlop Rubber, Australia, Ltd., for donating the special blankets used in this procedure, and in particular to Messrs. Waring and Sharpe of that firm for the time and trouble involved in developing a satisfactory set of blankets for our requirements.

We pay tribute to Mr. V. R. Ebsary, whose ingenuity and initiative were responsible for the development of the hypothermia equipment. This ingeniously contrived machine has done all that has been required of it in every case in which it has been used. In addition, Mr. Ebsary has attended, in every case in which hypothermia has been employed, to operate the machine for us. Although the machine is simple to use, his skilful regulation of the body temperature has relieved the anaesthetic and surgical staff from any worries in this regard, and has allowed us to concentrate wholly on the medical aspects of the particular case.

Finally, we recognize the contribution of Mr. A. Harper, of the Commonwealth Scientific and Industrial Research Organization, who also gave willingly of his time and knowledge to advise us on certain technical aspects of heat transference, and who kindly attended the theatre for the first few cases to assist in the organization and supervision of this procedure.

REFERENCES

Bailey, C. P., Cookson, B. A., Downing, D. F., and Neptune, W. B. (1954). *J. thorac. Surg.*, **27**, 73.
Bigelow, W. G., Lindsay, W. K., and Greenwood, W. F. (1950). *Ann. Surg.*, **132**, 849.
Brock, R. (1956). *Proc. roy. Soc. Med.*, **49**, 347.
Cooper, K. E., and Kenyon, J. R. (1957). *Brit. J. Surg.*, **44**, 616.
Delorme, E. J. (1952). *Lancet*, **2**, 914.
—— (1956). *Proc. roy. Soc. Med.*, **49**, 368.
Dundee, J. W., Gray, T. C., Mesham, P. R., and Scott, W. E. B. (1953). *Brit. med. J.*, **2**, 1237.
Khalil, H. H. (1957). *Lancet*, **1**, 185.
Lewis, F. J., and Taufic, M. (1953). *Surgery*, **33**, 52.
Lucas, B. G. B. (1955). *Med. Press*, **233**, No. 6055.
—— (1956). *Proc. roy. Soc. Med.*, **49**, 345.
—— (1958). *Brit. med. Bull.*, **14**, 46.
Ripstein, C. B., Friedgood, C. E., and Solomon, N. (1954). *Surgery*, **35**, 98.
Ross, D. N. (1954). *Lancet*, **1**, 1108.
—— (1956). *Proc. roy. Soc. Med.*, **49**, 365.
Swan, H., Zeavin, I., Holmes, J. H., and Montgomery, V. (1953). *Ann. Surg.*, **138**, 360.

TEMPERATURE GRADIENTS DURING HYPOTHERMIA

BY

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The most commonly used method of reducing the body temperature is by the surface cooling of an anaesthetized subject. A well-controlled method (Cohen and Hercus, 1959) has been used by us in all cases requiring hypothermia for cardiac surgery. Although much experimental work on various aspects of hypothermia has been done, we have been unable to find any record of studies having been made of the changes in temperature of the cerebral cortex in relation to temperature changes occurring simultaneously in other parts of the body. This investigation was undertaken in order to find out what part of the body will reflect most closely the changes in temperature occurring in the cerebral cortex during cooling, stabilization, and rewarming.

*Aided by a grant from the Royal Australasian College of Physicians.

Methods

Temperature measurements were taken with an electrical thermometer,† the calibration of which was checked before and during each set of readings. Six separate recordings were taken in the various sites, as listed, at intervals of two minutes. The nasopharyngeal temperature was measured with a mercury thermometer as an additional check on the accuracy of the readings. All leads, together with the mercury thermometers used, were previously calibrated against each other at temperatures of from 25° to 40° C, and were found to record to within 0.1° C. of each other throughout this range.

Cross-bred sheep, closely shorn, weighing 25–35 kg., were anaesthetized with intravenous sodium pentobarbitone and mechanically ventilated.

Leads containing thermistors were then connected to the animal for temperature-recording in the following sites:

1. *Cerebral Cortex.*—A small drill-hole was made in the skull at the postero-medial aspect of the base of the horn. A needle with a thermojunction at its tip was inserted through this hole direct into the cerebral cortex to its full length of 5 cm. It had previously been found, using a bisected sheep's head with the brain *in situ*, that insertion of the special lead (type K8) in this manner would result in the tip of the needle, containing the thermistor, being well within the brain substance.

2. *Central Blood Stream.*—The jugular vein was opened and a lead passed down it to the vicinity of the right atrium.

3. *Oesophageal.* — A standard lead was inserted approximately 30 cm. from the teeth, into the lower third of the oesophagus.

4. *Rectal.*—The large rectal lead was placed 7 cm. within the rectum.

5. *Nasopharyngeal.* — A recording was made of this temperature, using a mercury thermometer, some 6 to 8 cm. from the nostril.

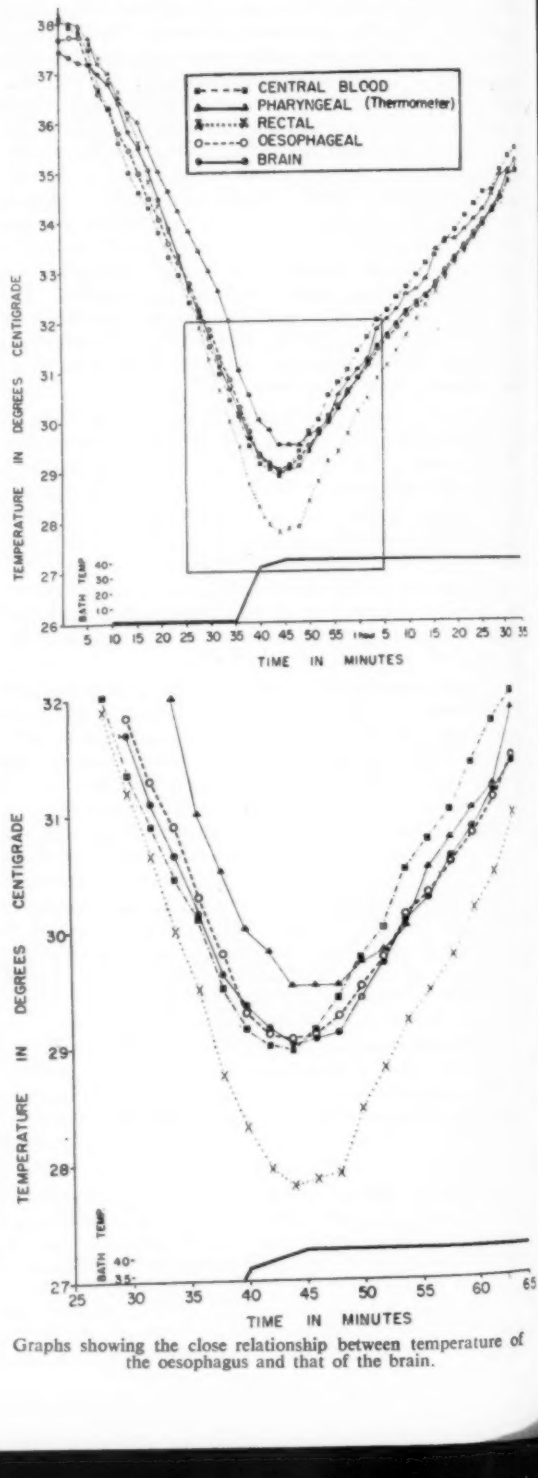
6. *Subcutaneous.*—A lead was left in the subcutaneous tissues of the neck. As expected, the temperatures recorded at this site bore little relation to the other readings and merely served to indicate that peripheral temperature records are without value as an indication of central blood or brain temperature during hypothermia; consequently they are not shown in the Graphs, as they would result in unnecessary complication.

All leads were firmly fixed in position, then the animal was placed in a bath and covered with iced water at 1–2° C. The water was constantly agitated and simultaneous readings were taken from each lead. These were recorded in graph form, together with the bath temperature, at intervals of two minutes (see Graphs). The temperature of the animal, as recorded in the cerebral cortex, was reduced to 29–30° C., and either allowed to drift and stabilize before rewarming or the animal was actively rewarmed in water at 41–42° C. immediately after the cooling was finished.

The results (see Graphs) show how closely the temperature recorded in the lower third of the oesophagus reflected the temperature of the cerebral cortex, this relationship being maintained during cooling, stabilization, and rewarming. As expected, the blood-stream temperature was cooler than the brain during cooling and warmer during rewarming. The rectal and nasopharyngeal temperatures were not so informative as the oesophageal reading, since they both reflected changes in the blood and brain temperatures very sluggishly.

Discussion

The chief reason for using hypothermia in cardiac surgery is to enable an arrest of the whole or part of the circulation so that the surgeon can perform some task that would be difficult or impossible at normal



Graphs showing the close relationship between temperature of the oesophagus and that of the brain.

†The Electric Universal Thermometer, type T.E.3, manufactured by Elektrolaboratoriet, Copenhagen, utilizing leads types H1, R1, R7, and K8.

temperatures. The safe duration of this circulatory arrest is limited by the viability of the central nervous system—the lower the temperature the longer being the time available (Lucas, 1956). The actual temperature of the brain at the moment that blood flow to it is stopped is the all-important factor in determining the safe period of circulatory arrest. Hitherto it has been assumed that the temperature of the brain substance is reflected closely by that recorded in the nasopharynx (Ross, 1956) or oesophagus (Lucas, 1958), but no actual temperature recording of the cerebral cortex has been shown. Cooper and Kenyon (1957) stated that the rectal and oesophageal temperatures crossed only during rewarming, but we have found in all cases, both clinical and experimental, that the rectal temperature invariably crossed the oesophageal temperature either during cooling or during stabilization, and fell well below it with a large and variable overswing; then, during rewarming, it again always recrossed the oesophageal temperature.

The large drift, or overswing, of the rectal temperature is probably partly due to the rectal contents forming a storage of cold or heat. In addition blood from the skin around the perineum returns to the body via the haemorrhoidal veins, and this blood, during cooling, is much colder than the central blood. This blood must cool the rectal wall and its contents more than the rest of the body and will accentuate the cold-storage effect mentioned above. We have observed that the overswing in temperature and the delay in reflecting temperature changes are often roughly proportional to the quantity of rectal contents.

When the bath is emptied the rectum takes some 15–20 minutes to reach a stable temperature, whereas the central blood, oesophagus, and brain stabilize within five minutes.

Also, when the water in the bath is quickly warmed to 40–42° C. and maintained at this level, after first cooling the animal to 30° C., the brain, central blood stream, and lower oesophageal readings will show a change from cooling to rewarming within five minutes; yet the rectal temperature will continue to fall for ten minutes or more until it sluggishly reflects the changes already obvious in the other leads.

The blood temperature in these experiments is that recorded in the vicinity of the right atrium, and it is probably slightly cooler than the aortic blood during cooling and slightly warmer than it during rewarming. The amount of heat exchange that doubtless occurs after the blood leaves the right heart and passes through the pulmonary circulation prior to entering the left heart and aorta would tend to reduce the gradient between the venous blood temperature, as measured at the right atrium, and the brain temperature.

Cooper and Kenyon (1957) have shown that the oesophageal temperature closely followed the para-aortic temperature during surface cooling by ice-bags, and we have found in clinical cases that the aortic blood temperature is always within 0.2° C. of the temperature in the lower oesophagus (Cohen and Hercus, 1959).

In other words, it is reasonable to assume that the temperature of the brain, the central arterial blood, and the lower oesophagus will always correspond during cooling, stabilization, and rewarming.

The observation that the temperature in the lower third of the oesophagus so closely parallels that of the cerebral cortex during both cooling and rewarming is most helpful. Whenever hypothermia is employed we can proceed confidently to interrupt the blood supply to the brain, knowing with certainty its temperature at that particular moment.

Hitherto it has been assumed that the temperature of the mid-oesophagus (Delorme, 1956; Lucas, 1958) or the nasopharynx (Brock, 1956) gave a reasonably accurate assessment of the cerebral temperature. The nasopharynx is observed to be unreliable, but it always errs on the "safe" side. Even so, this is undesirable, as unnecessary extra cooling will be undertaken, and this is potentially dangerous.

The mid-oesophagus is more satisfactory, but is still not so accurate as the lower oesophagus in reflecting changes in brain temperature. In clinical cases it is important to ensure that the oesophageal lead is accurately located in the lower third of the oesophagus before proceeding. This is done by carefully measuring the distance that the lead is to be inserted and then moving it both up and down a short distance and checking the reading, as under anaesthesia the readings both in the mid-oesophagus and in the upper part of the stomach will be found to be slightly higher than when the lead has been correctly sited in the lower oesophagus. As cooling is proceeding it may be advisable to move the lead up and down the oesophagus to check the position again; its lower third will be found the coolest place.

Peirce (1958) has shown that cooling induced during extracorporeal circulation results in temperature changes in the brain and oesophagus being almost identical. This confirms our observations during surface cooling.

Summary

Simultaneous temperature records have been taken in the rectum, oesophagus (lower third), nasopharynx, right atrium, and cerebral cortex during hypothermia and rewarming.

The close correlation between the temperature in the lower third of the oesophagus and the cerebral cortex makes it the logical site from which to record the body temperature during hypothermia.

We thank Dr. D. S. Stewart for generously making available facilities at the McMaster Animal Health Laboratory. Mr. F. Hamilton gave us invaluable assistance with the preparation, handling, and anaesthesia of the animals.

REFERENCES

Brock, R. (1956). *Proc. roy. Soc. Med.*, **49**, 347.
Cohen, D., and Hercus, V. (1959). *Brit. med. J.*, **1**, 1435.
Cooper, K. E., and Kenyon, J. R. (1957). *Brit. J. Surg.*, **44**, 616.
Delorme, E. J. (1956). *Proc. roy. Soc. Med.*, **49**, 368.
Lucas, B. G. B. (1956). Ibid., **49**, 345.
—— (1958). *Brit. med. Bull.*, **14**, 46.
Peirce, E. C. (1958). In *Extracorporeal Circulation*, edited by J. G. Allen, p. 221. Thomas, Springfield, Illinois.
Ross, D. N. (1956). *Proc. roy. Soc. Med.*, **49**, 365.

The Argentine medical journal *El Día Médico* has dedicated a special number to British medicine, sponsored by the British Ambassador in Buenos Aires, Sir JOHN WARD. It is part of the journal's policy to produce such an issue each year on, for example, overseas medicine, congresses, or symposia. The present issue includes articles by Professor CHARLES NEWMAN, Dr. FRANK H. LUMB and Professor MAX ROSENHEIM, Sir CHARLES HARINGTON, Professor NOEL MACLAGAN, Dr. NORMAN MCKAY, and Dr. NIGEL G. TROTT, Mr. T. HOLMES SELLORS, Dr. A. TALBOT ROGERS, and Dr. F. AVERY JONES. A brief account of the National Health Service is also included.

STUDIES IN THE EPIDEMIOLOGY OF TINEA PEDIS

I. TINEA PEDIS IN SCHOOL CHILDREN

BY

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Although there are numerous reports of the incidence and epidemiology of tinea pedis in skin clinics, closed communities, and industrial groups, the natural history of this disease in the general population has received very little study.

The difficulty of examining a representative cross-section of adults is obvious, apart from the prohibitive amount of time which would be involved in visiting sufficient families in their own homes. Also, in adults, the past lives of individuals would be so varied that any results obtained would be very difficult to assess.

Investigation of recruits for the Forces or of first-year university students has a number of limitations, the greatest being that the subjects are drawn from widely scattered geographic areas, so that results would show the incidence rather than the epidemiology of the disease.

A cross-section of the children resident in any one district can, however, be obtained by carrying out surveys in comprehensive and bilateral schools and, to a less extent, in secondary modern schools. The study of day-school children has the further advantage that they have usually lived exclusively within their families and in the district in which the school is situated; also, the difference in the way of life of the sexes is far less marked than in adults.

Examination of school children might therefore throw a useful light on the epidemiology of tinea pedis. We can find no record of any such survey in the United Kingdom. In Europe large-scale investigations have been carried out by Lomholt (1938) in Sweden, and by Wilde (1951) and Polemann (1955) in Germany, but their conclusions were based almost exclusively on clinical evidence. Amrein (1953), in Switzerland, examined 707 children and confirmed his clinical diagnosis by microscopical examination of scrapings, but he made no cultures and did not differentiate between the incidence in boys and girls. Bocobo and Garcia (1950), using laboratory diagnostic tests, examined 203 Philippine students between 11 and 22 years old, but did not correlate incidence with age. In America, Andrews and Birkman (1931) and Wallace and Moorman (1943) examined 520 and 60 children respectively, but in neither investigation were conditions comparable with those in schools in this country.

The present investigation sets out to study aspects of the natural history of tinea pedis through the medium of Bristol's school children, to obtain some factual information on a number of epidemiological problems about which there is at present much guesswork, and to open up lines for more detailed work later.

The Subjects

Approximately 300 children were examined in each of six secondary modern boys' schools (schools 1–6), six secondary modern girls' schools (schools 7–12), and four junior boys' schools (schools 13–16). Small numbers of children of grammar-school standard were seen in four of the modern schools. Pupils in junior schools were aged 7–10 years, those in senior schools 11–14 years. Teachers were asked to produce about 80 children from each year with no attempt at statistically random sampling. However, they normally produced a whole class at a time.

The schools were selected from among those using three Corporation swimming-baths in widely separated parts of Bristol, two senior boys' schools and two senior girls' schools to each bath, and two junior boys' schools in each of two of the districts (Table I). Bath A was situated in district A and attended by schools 1, 2, 7, 8, 13, and 14; bath B was in district B and attended by schools 3, 4, 9, and 10; and bath C was in district C and used by schools 5, 6, 11, and 12. Schools 15 and 16, while situated in district B and passing many of their pupils to schools 3 and 4, did not attend the same swimming-bath as the latter schools. Bath B was closed in winter, and schools 4 and 10 used an alternative one during this time.

TABLE I.—*Showing Location of Schools in Relation to Districts and Swimming-baths*

District	Bath	Schools Using Bath		
		Senior Boys	Senior Girls	Junior Boys
A	A	1 and 2	7 and 8	13 and 14
B	B*	3 ,, 4	9 ,, 10	(15 ,, 16†)
C	C	5 ,, 6	11 ,, 12	

* Bath B is closed in winter, when schools 4 and 10 use an alternative one.
† Schools 15 and 16, though situated in District B, and passing many of their pupils to schools 3 and 4, did not use the same swimming-bath as the latter.

Methods

The survey was carried out in the winter and spring of 1956–7. The organization of the school visits and the screening of the children's feet were carried out exclusively by one of us (M. D. G.). The other (M. P. E.) was responsible for the laboratory work and also took most of the scrapings. Relevant personal details were taken down from the children by a clerical assistant.

The children's feet were classified according to their condition and the type of lesion into Holmes and Gentles's (1956) first five groups. Where the only blemish was plantar warts, blisters, or other injury, feet were taken as "normal" for our purposes. The distinction between a normal foot and one with a very slight lesion was in practice extremely difficult to make, especially in the smaller children, and a certain variation in judgment was inevitable.

As the time available, both to the schools and to ourselves, was limited, scrapings were taken as a routine only from children with lesions.

Feet were not cleaned before being scraped and no record of diseased toenails was made. A few children were under treatment for tinea pedis, diagnosed on purely clinical grounds. It was impossible to determine whether failure to recover dermatophytes from some of these was due to faulty diagnosis in the first place or to destruction of the fungi by treatment.

Scrapings were taken from both feet, from different lesions, and from different parts of large lesions, on to a piece of clean paper. From the smaller lesions, and especially from the younger children, it was often impossible to obtain enough material for both culture

and microscopical examination. In view of the experience of Gentles and Dawson (1956), who were also investigating skin lesions only, cultural procedures were given priority, and microscopical examination of scrapings in 15% potassium hydroxide was made only when there was enough surplus material—that is, for 64% of the senior children with lesions and 58% of the junior. Strauss and Kligman (1957) found examination in potassium hydroxide superior to culture; but a large proportion of their specimens were toenails, from which we too, in other work, have found cultures difficult to obtain.

Cultures were made on glucose–peptone agar with added penicillin and streptomycin. Where possible, from 12 to 20 inoculations were made from each subject. Little trouble was experienced from saprophytic bacteria or fungi.

Results

Two limitations of our method affect all our results. The first concerns specimens that were too small to allow for microscopical examination. Of 617 of these, 38 (6.2%) were mycologically positive, while 138 (13.2%) of 1,048 scrapings which were examined microscopically were positive. Of the latter, 13 would have been missed without the aid of microscopical examination. Supposing that the same proportion of positives among the small specimens had been overlooked for this reason, the proportion of positives in the group would have been raised only from 6.2% to 7.5%. Statistically the probability of such a difference happening by chance is less than 1 in 1,000; therefore it is highly likely that there is a real difference in the infection rate of large and small lesions.

The effect of the omission of routine examination of normal feet must also be considered. This would result in our overlooking the lesion-free carriers reported by other workers. Also, if the number of carriers in the child population were uniform we would miss proportionally more infections in schools where more children had normal feet. To gauge the magnitude of this error we took scrapings at the end of the survey from the interdigital spaces of the feet of two groups, each of about 100 normal children, in schools with high and low incidences respectively as based on our findings in children with lesions (Table II).

TABLE II.—*Percentage of Symptomless Carriers*

Amount of Infection in Children with Lesions	Total Screened	Children with No Lesions			Symptomless Carriers
		Total in School	Total Mycologically Examined	No. Infected	
8·9%	628	343	109	3	1·5%
2·2%	365	253	83	0	0·0%

In schools with a high incidence 1.5% of carriers were found, and in those with a low incidence no cases were found in the 83 children examined. The difference is not statistically significant. The number of carriers disclosed by this sample is not high enough to distort our results significantly, and the tendency shown for the occurrence of more lesion-free carriers in populations with a high incidence of infection would emphasize our findings rather than minimize them. It seems probable that these carriers usually represent incipient or almost resolved infections, a proportion of which one would expect to find in any infected population, especially where the disease rate is high (Strauss and Kligman, 1957).

Relationship of Lesions and Infection to District, School, and Sex (Table III). — Of 4,794 children screened, 1,664 (34.7%) had lesions and 176 (3.6%) were infected with tinea pedis. The incidence of lesions in senior boys (40.3%), was significantly higher than in junior boys (33.2%) or senior girls (30.4%). The incidence of infection among senior boys (6.6%) was significantly higher than that in the other two groups—2.2% and 1.6% respectively. There was, however, a wide variation in infection among those with lesions, the incidence of infected lesions varying from 5.4% in senior girls to 16.5% in senior boys, and from 0.0% in schools 11 and 16 to 22.6% in school 2. The incidence of lesions varied greatly from school to school and was not related to district. But the incidence of infection in both senior (8.9%) and junior (3.1%) boys' schools in district A was significantly higher than in similar schools in the other districts, which averaged 5.5% and 0.5% respectively. There was no significant difference in infection between schools of the same type in any one district. Among girls the incidence of infection was too low for any significance of the effect of district to be calculable.

TABLE III.—*Incidence of Lesions and of Infection According to District, School, and Sex*

	District	School	No. of Children Screened	With Lesions		Infected		% of those with Lesions Infected
				No.	%	No.	%	
Senior boys	A	1	292	152	52	26	8·9	17·1
		2	336	133	40	30	8·9	22·6
	B	3	306	110	36	18	5·9	16·4
		4	284	123	43	18	6·3	14·6
	C	5	336	122	36	15	4·5	12·3
		6	285	101	35	15	5·3	14·9
		Total	1,839	741	40·3	122	6·6	16·5
Senior girls	A	7	414	111	27	8	1·9	7·2
		8	365	112	31	8	2·2	7·1
	B	9	315	70	22	2	0·6	2·9
		10	448	143	32	7	1·6	4·9
	C	11	225	73	32	0	0·0	0·0
		12	294	117	40	9	3·1	7·7
		Total	2,061	626	30·4	34	1·6	5·4
Junior boys	A	13	310	99	32	13	4·2	13·1
		14	234	93	40	5	2·1	5·4
	B	15	214	67	31	2	0·9	3·0
		16	136	38	28	0	0·0	0·0
		Total	894	297	33·2	20	2·2	6·7
All children			4,794	1,664	34·7	176	3·6	11·6

Effect of Age on Incidence of Lesions.—Fig. 1 shows that the incidence of lesions increased with age in both

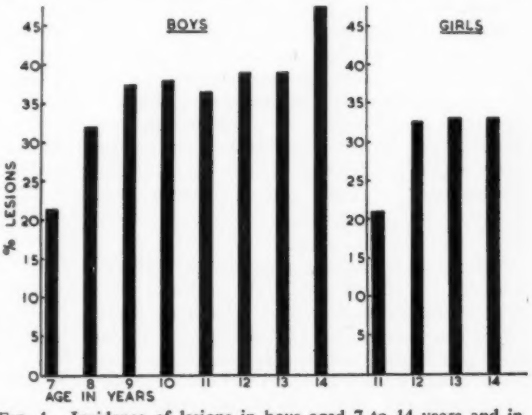

FIG. 1.—Incidence of lesions in boys aged 7 to 14 years and in girls aged 11 to 14.

sexes, but was always less in girls than in boys of the same age. In boys there were sudden significant ($p<0.02$) increases between the ages of 7 and 8, and of 13 and 14; and in girls between 11 and 12 there was also a highly significant increase: none of these could be explained by any change in personal or social conditions at these ages.

Effect of Age on Incidence of Infection.—Fig. 2 shows that boys as young as 7 years can become infected and that the total incidence rose from 0.6% at this age

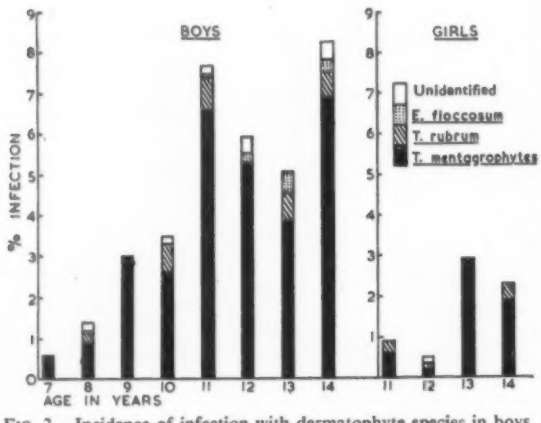

FIG. 2.—Incidence of infection with dermatophyte species in boys aged 7 to 14 years and in girls aged 11 to 14.

to 7.7% at 11 years, the age of transfer to the senior school. There was a marked increase in *Trichophyton mentagrophytes* infection between the ages of 8 and 9. After age 11 the incidence of infection dropped, to rise again to 8.3% at 14. The high incidence at ages 11 and 14 might be attributed to "epidemic years," but this idea requires further investigation. Puberty did not appear to affect the incidence of infection, which was already high at 11 years. Incidence was very low in all senior girls, but a statistically significant increase did occur between girls under 13 and those over 13.

Effect of Cleanliness and Social Status.—Visits to schools were made on the same day of each week and without warning the children beforehand. It is therefore probable that we saw our subjects, with some constancy, in their normal state of cleanliness. During screening, all children with foot lesions and 979 of those without were classified as clean, fair, or dirty, judgment being based on ingrained rather than superficial dirt and on the condition of the toenails. No statistical association, as indicated by the χ^2 test, was found between cleanliness and either lesions or infection. Most schools drew their pupils from socially mixed areas, but in the three which served almost exclusively a poorer type of family (3, 9, and 16) the incidence of tinea pedis was of the same order as that in similar schools in the same district serving socially mixed areas.

Association of Infection with Type of Lesion.—90% of lesions fell into Holmes and Gentles's (1956) group II (peeling and/or maceration). Most of the remainder were classed in group III (erythema or fissures), and group V (vesicles) was hardly ever seen. These figures differ radically from those for miners, and are such that it is statistically impossible to correlate infection with any particular type of lesion.

Infection and Use of Swimming-baths and School Showers.—In the senior schools, for both sexes (with the exception of school 9 with 44% bathers), 67 to 96% of children attended school swimming-classes. There was no significant correlation for boys between infection and attendance at these classes. For girls, infection was significantly higher among non-bathers, indicating the preponderance of some other source of infection for them. Though the difference in the proportion of boys and girls attending swimming-classes is too slight to account for the different incidence of tinea pedis in the sexes, records kept at the swimming-baths show that there are three times as many total admittances of boys as of girls. This implies a much more frequent use of baths by boys out of school hours. Senior schools in districts A and C (excepting school 7) possessed showers; schools in district B had none. But no correlation was found between infection and the use of school showers by individual children, or between incidence in any school and the presence or absence of showers. However, senior boys' schools 1 and 2, with 8.9% infection each, were the only ones where swimming-classes were held all the year round throughout the school, and which also possessed showers. Schools 3–6, with infection rates of from 4.5% to 6.3%, either lacked showers (3 and 4), went to swimming-baths only in the summer (3), or went in the lower forms only (5 and 6). There was no similar relationship in girls' schools. An investigation into the occurrence of dermatophytes on the floors of swimming-baths is reported in this issue (English and Gibson, 1959). It may be mentioned here that *T. mentagrophytes* was isolated from the floors of all the baths.

Footwear.—"Daps" (canvas shoes with rubber soles) are issued to all children for physical education classes. At the end of the school year they are collected, sterilized by exposure to formalin vapour, and stored for reissue to different children the following year. Laboratory tests indicated that this routine sterilization was probably adequate, and we do not consider that the reissue of daps is a serious source of infection. Exchange of shoes among children is, however, inevitable, and doubtless accounts for some cases of tinea pedis. Certain physical education classes in some schools are taken with bare feet, and must also provide a risk of infection.

Mycology

Table IV shows that *T. mentagrophytes*, the *interdigitale* type of which was consistently isolated, was responsible for the overwhelming majority of cases of tinea pedis in Bristol school children (84.4%). This was true for all schools, districts, and ages, and for both sexes. The fungus was found eight times more often

TABLE IV.—*Incidence of Species of Dermatophytes, Including Those Found in the Sample of Lesion-free Children*

Type of School	Total Children Screened	Cases of *T. mentagrophytes*		Cases of *T. rubrum*		Cases of *E. floccosum*		Cases Microscopically Positive Only	
		No.	%	No.	%	No.	%	No.	%
Junior boys	894	17	1·9	1	0·1	0	0	2	0·2
Senior ,,	1,839	106*	5·8	8	0·4	7*	0·4	5	0·3
,, girls	2,061	29	1·4	4	0·2	0	0	1	0·05
All ..	4,794	152	84·4	13	7·2	7	3·9	8	4·4

* Including one combined infection of *T. mentagrophytes* and *E. floccosum*. This occurred in school 2, with a high total infection rate and four out of the six other *E. floccosum* infections.

than *T. rubrum* and *E. floccosum* together. This is in marked contrast to figures from skin clinics both in England and abroad, where the proportion of *T. rubrum* infections is much higher. For instance, in the dermatological clinic of the Bristol General Hospital, from 1954 to 1957, *T. mentagrophytes* and *T. rubrum* have each been responsible for 57 cases of tinea pedis. The discrepancy arises because the chronic and disfiguring nature of *T. rubrum* infections leads to the reference of a high proportion of them for specialist advice.

T. rubrum was found twice as often as *E. floccosum* and occurred in most schools, at all ages, and in both sexes. *E. floccosum* was found only in senior boys, and its incidence in this group was equal to that of *T. rubrum*. The proportion of boys to girls among those aged 11–14 years with *T. mentagrophytes* infection was 4:1; for *T. rubrum* the proportion in the sexes was 2:1.

Discussion and Conclusions

Despite limitations of method, the results of this survey clarify a little our picture of the epidemiology of tinea pedis. In the first place the choice of day-school children as subjects limited the size of the problem and has resulted in the focusing of attention on certain factors influencing the disease while eliminating a number of others previously believed to do so.

The striking difference we have found between the incidence of lesions and of true tinea pedis confirms the results of Holmes and Gentles (1956) and other workers, and lays emphasis on the necessity of laboratory examination for the accurate diagnosis of the disease. For example, Wilde (1951) and Polemann (1955), working with German children and using clinical diagnosis only, obtained figures for "infection" which are of the same order as ours for lesions; while Amrein (1953), using microscopical examination of scrapings, obtained an average infection rate of 4.1% for Swiss urban children, which compares closely with our average of 3.7%.

The following epidemiological discussion refers to *T. mentagrophytes* only, as this fungus has been shown to be of dominant importance in Bristol children.

Two points need elucidation. First, what factors in, or habits of, the individual predispose him to infection? This question includes the problem of the different incidence in the sexes. Age in itself in young people is probably not a factor. The increase of incidence with age is most likely simply a reflection of the increased opportunity for infection (Wilde, 1951).

There have been varying opinions on the effect of hygiene. Polemann (1955) and Andrews and Birkman (1931) claim that washing encourages the fungus, while Wallace and Moorman (1943) and Bocobo and Garcia (1950) consider that it thrives in dirt. These observations were either mere opinions or were based on small numbers of cases. The rating of cleanliness must be subjective and inexact, but our results are based on sufficient numbers to suggest that there is in fact no relationship between cleanliness and liability to be infected.

Neither does the incidence of infection in boys lend credence to the common belief that tinea pedis is a rare disease before puberty. Nor is the incidence materially affected by social status. If the presence of lesions of undetermined aetiology predisposes the feet to infection, the higher incidence of such lesions in boys might account for their higher infection rate. But the fact that the percentage of *infected* lesions differs widely in different schools seems to dispose of this as a major factor affecting incidence.

Tritsmans and Vanbreuseghem (1955) have shown that there is a positive correlation between tinea pedis and the frequency of use of swimming-baths. Though we found no relationship between incidence of the disease and attendance at school swimming-classes, there is evidence that boys swim more frequently than girls out of school hours, and that boys' schools where the curriculum includes swimming summer and winter throughout the school career (schools 1, 2, and 4) have a higher infection rate than those whose pupils swim less continuously. These observations, and any differences in the normal footwear of boys and girls, obviously require detailed investigation.

It still remains possible that some unknown physiological factor is responsible for the different incidence in the sexes.

The second point needing an explanation is—where does the main source of infection lie and how is the disease spread?

Children are exposed to three main sources of infection—the family, the school, and the swimming-bath. Previous work (English, 1957) has shown that they run a serious risk of contracting *T. rubrum* infection should it be present in the family: a similar survey is being carried out for *T. mentagrophytes*.

In school there is a theoretical risk from a number of sources. The practice of reissuing sterilized daps can probably not be incriminated, though bare-foot gymnastics and the borrowing of footwear must spread infection. But the former occurs in all schools and the latter is not a common practice, so that neither would account for different incidences in different districts.

In view of the findings of Holmes and Gentles (1956), school showers must certainly be involved, and further investigation into their use is necessary, but as each child uses them approximately only twice weekly the risk cannot be compared with that in pithead baths used daily by the miners. Though there is some indication that, combined with frequent swimming, they tend to increase infection, they do not appear to be a major risk in schools, as we have been unable to correlate the use of them with a high incidence of tinea pedis.

There is, however, a strongly positive correlation between geographic area and tinea pedis in boys' schools, for which the local swimming-bath and the frequency of its use by schools in the district are the only probable explanation. This, together with frequent use of the baths out of school hours by boys, and the results of investigations in the baths themselves (English and Gibson, 1959), incline us, pending further information, to the opinion of Amrein (1953) that the swimming-bath is an important focus of fungal infection of the feet in school children.

Summary

1,839 boys and 2,061 girls, aged 11–14, from 12 secondary modern schools, and 894 boys, aged 7–10, in four junior schools, all situated in three different districts of Bristol, were examined for tinea pedis.

Of the senior boys 40.3% had lesions and 6.6% had tinea pedis; 30.4% of senior girls had lesions and 1.6% tinea pedis; 33.2% of junior boys had lesions and 2.2% were infected.

In the girls the incidence was too low to allow correlation of results with relevant environmental factors.

In the boys the incidence of tinea pedis increased gradually to age 11 and then fluctuated irregularly.

No correlation was found between infection rate and cleanliness, the presence of non-mycotic lesions, social class, or the use of school showers.

There was a marked correlation between infection and the district in which the schools were situated. Senior and junior boys' schools in district A had 8.9% and 3.1% infection respectively: similar schools in districts B and C together had 5.5% and 0.4% infection respectively. It is concluded the local swimming-baths and the frequency with which they are used are the probable cause of this.

Of the 179 infections, 84.4% were caused by *Trichophyton mentagrophytes*, 7.2% by *T. rubrum*, 3.9% by *Epidermophyton floccosum*, and 4.4% were identified by microscopical examination only.

We acknowledge the kindness of the head teachers and staffs of the schools, without whose co-operation this investigation would have been impossible. We are indebted to Miss E. H. L. Duncan, of the Central Health Clinic, Bristol, for guidance and practical help in the statistics. Our thanks are also due to Dr. R. P. Warin and Dr. C. D. Evans, of Bristol Royal Hospital, and to Dr. R. C. Wofinden, medical officer of health, Bristol, for their advice and encouragement.

ADDENDUM.—Since writing this paper our attention has been drawn to Scheffler's (1958) investigation of tinea pedis in 2,622 German school children. Though differing from ours in the wider age range of the children and in slightly more restricted criteria for selection of those for scraping, the results should be roughly comparable. In fact, Scheffler's total incidence of infection of 3.4%, as determined by microscopical examination, is remarkably similar to ours, but the incidence in the sexes, determined microscopically, differs in being almost equal in boys and girls. However, the dominant fungus among Scheffler's subjects is *T. rubrum* (79% of 67 cultures obtained); and indications in our survey and in the investigation of this fungus in families (English, 1957) are that the incidence of *T. rubrum* in females far more nearly approaches that in males than is the case for *T. mentagrophytes*. Scheffler's results support this observation. Unfortunately Scheffler does not give the incidence of the fungus species in the sexes; nor does he relate his mycological findings to age.

REFERENCES

Amrein, H. P. (1953). *Praxis*, **42**, 197.
Andrews, G. C., and Birkman, F. W. (1931). *N.Y. St. J. Med.*, **31**, 1029.
Bocobo, F. C., and Garcia, D. (1950). *J. Philipp. med. Ass.*, **26**, 169.
English, Mary P. (1957). *Brit. med. J.*, **1**, 744.
—— and Gibson, Mary D. (1959). Ibid., **1**, 1446.
Gentles, J. C., and Dawson, Christine O. (1956). *Trans. Brit. mycol. Soc.*, **39**, 465.
Holmes, J. G., and Gentles, J. C. (1956). *Lancet*, **2**, 62.
Lomholt, S. (1938). *Med. Klin.*, **34**, 118.
Polemann, G. (1955). *Arch. klin. exp. Derm.*, **201**, 24.
Scheffler, H. S. F. (1958). *Mykosen*, **1**, 102.
Strauss, J. S., and Kligman, A. M. (1957). *A.M.A. Arch. Derm.*, **76**, 70.
Tritsmans, E., and Vanbreuseghem, R. (1955). *Belg. T. Geneesk.*, **11**, 625.
Wallace, G. I., and Moorman, H. E. (1943). *Arch. Derm. Syph. (Chicago)*, **47**, 816.
Wilde, H. (1951). *Z. Haut- u. Geschl.-Kr.*, **10**, 99.

STUDIES IN THE EPIDEMIOLOGY OF TINEA PEDIS

II. DERMATOPHYTES ON THE FLOORS OF SWIMMING-BATHS

BY

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The results of a recent investigation into the epidemiology of tinea pedis in Bristol school children (English and Gibson, 1959) suggested that the public swimming-baths were an important source of transmission of this infection.

Amrein (1953) found that school children in Zurich, with access to public swimming-baths, showed nearly the same percentage of infection as was found in the Bristol children, but that those from remote mountain villages with no public bathing facilities had no infection with tinea pedis. Amrein did not report any attempt to isolate dermatophytes from the floors of the baths.

Tritsmans and Vanbreuseghem (1955), in Belgium, showed that 30% of persons whose main recreation was swimming in public baths had tinea pedis, compared with 4.5% of gymnasts and 3.5% of a control group. They failed, however, to grow dermatophytes from material scraped from the floors of the swimming-baths used by their subjects. Attempts to isolate these fungi from the floors of shower-baths in the United States by similar sampling methods (Ajello and Getz, 1954; and other workers) have had disappointing results.

However, Gentles (1956) has developed a direct sampling technique, which he used with considerable success on the floors of pithead baths, and this method has been adopted for the examination of three swimming-baths in Bristol.

The swimming-baths investigated were baths A, B, and C, used by the school children examined in our survey of tinea pedis (English and Gibson, 1959).

Baths A and C were so laid out that the accommodation for changing opened on to passages from which the only access to the pool itself was through footbaths filled with chlorinated water. In bath B the cubicles opened straight on to the side of the pool. Sampling of the changing accommodation included showers, lavatories, passages, and wooden slats, where they existed, as well as the floors of the cubicles. Floors were made from smooth tiles patterned with grooves, with a strip of concrete 1 ft. (30 cm.) wide surrounding the pool.

All baths were cleaned twice daily with brooms and a solution of "chloros." In addition, baths B and C were sluiced down with buckets of water frequently during the day. Bath A was not sluiced.

Procedure and Methods

Sampling was carried out during those parts of the school term falling in the period July to October, 1957. Samples were taken at 9 a.m., before the admission of bathers, and at approximately 4 p.m., up to which time the great majority of bathers were organized school

parties. Morning and afternoon samples were not taken on the same days or from precisely the same positions.

The sterile velvet-covered sampling-pads were used as described by Gentles (1956), except that the basic culture medium on to which they were stamped was glucose (4%)–peptone (1%) agar, to which the antibiotics were added. Where floors were dry they were damped with fresh water before sampling. Results were recorded in terms both of the number of pads used and of the number of colonies isolated.

In addition, cultures were made from scrapings from the feet of all swimming-bath employees.

Results

Contamination of Baths

The *interdigitale* type of *Trichophyton mentagrophytes* was the only dermatophyte isolated from the floors.

Table I shows the findings for different areas of the three baths. In baths A and B the boys' changing accommodation, after use, was far more highly contaminated than that of the girls: in bath C the only colony isolated was on the boys' side. As the physical circumstances of the boys' and girls' sides in each bath are likely to be the same, it is probable that the difference in contamination between the two areas is a real one.

From the sides of the pools dermatophytes were obtained from only 3 pads out of the 33 used, a surprisingly low figure at first sight. It is probable, however, that the constant splashing would wash most small particles, including skin fragments, either into the grooves of the tiles or into the pools themselves. Such particles, therefore, would tend to be removed from contact both with the sampling-pads and with the bathers' feet in this area. This would also be the effect of sluicing.

The efficacy of routine cleaning methods was determined by sampling the most highly contaminated part of the baths, the boys' changing accommodation, before use. Only one pad out of 21 was contaminated, and the area from which this sample was taken was noticeably dirty. It would seem that established cleaning methods are adequate if conscientiously carried out.

There was a marked difference in the incidence of contamination in the baths, many more isolations and infected pads being obtained from bath A than from B or C. The possibility that some of the colonies in bath A were obtained from particles from the feet of one bather cannot be excluded.

There was no evidence of the superiority or otherwise of baths in which the cubicles opened on to a passage rather than on to the edge of the pool, for baths A and C, the most and least contaminated respectively, were both of the passage type.

Tinea Pedis Among Staff

Table II shows the results of the examination of the feet of swimming-bath staff. Swimming instructors and bath attendants wore plimsoll-type shoes for their work unless they were actually about to swim, yet 8 out of 14 if these harboured various dermatophytes, whereas none of the 11 who never entered the water were infected. Though *T. mentagrophytes* was the only fungus isolated from the bath floors it was found in only 3 out of 6 of the staff cases where the fungus was identified. Amrein (1953), working with larger numbers, also found a high incidence of tinea pedis in swimming-bath staff.

Discussion

Gentles's direct sampling technique has proved highly satisfactory for the isolation of *T. mentagrophytes* from floors, but *T. rubrum* and *Epidermophyton floccosum* were never found. This is probably partly due to the

TABLE I.—*Isolation of Dermatophytes from Swimming-baths*

Position of Sample	Bath A (Passage Type)			Bath B (No Passage)			Bath C (Passage Type)			Total		
	No. of Pads Used	No. of Pads Infected	No. of Colonies	No. of Pads Used	No. of Pads Infected	No. of Colonies	No. of Pads Used	No. of Pads Infected	No. of Colonies	No. of Pads Used	No. of Pads Infected	No. of Colonies
Boys' changing accommodation* (after 7–8 hours' use)	6	5	29	3	2	3	8	1	1	17	8	33
Sides of bath (after 7–8 hours' use)	12	2	3	9	1	3	12	0	0	33	3	6
Girls' changing accommodation* (after 7–8 hours' use)	8	1	1	6	0	0	3	0	0	17	1	1
All positions after use of baths	26	8	33	18	3	6	23	1	1	67	12	40
Boys' changing accommodation* (after cleaning)	6	0	0	6	1	2	9	0	0	21	1	2

* Including cubicles, lavatories, and, where present, showers and passages.

TABLE II.—*Tinea Pedis in Swimming-bath Staff*

Employment	Bath A			Bath B			Bath C			Total		
	Total Personnel	No. Infected	Fungus Isolated	Total Personnel	No. Infected	Fungus Isolated	Total Personnel	No. Infected	Fungus Isolated	Total Personnel	No. Infected	Fungus Isolated
Instructors	2	1	Microscopically +ve only	2	1	*T. mentagrophytes*	1	1	*T. mentagrophytes*	5	3	1 microscopically +ve only 2 *T. mentagrophytes*
Bath attendants	1	1	*T. rubrum*	5	2	1 *T. rubrum* 1 *E. floccosum*	3	2	1 microscopically +ve only. 1 *T. mentagrophytes*	9	5	1 microscopically +ve only. 1 *T. mentagrophytes*. 2 *T. rubrum*. 1 *E. floccosum*
Others (clerical and cleaning)	4	0	—	5	0	—	2	0	—	11	0	—

slow growth rate of these fungi making them more susceptible than *T. mentagrophytes* to overgrowth by other organisms on the culture plate. But the main reason would seem to be their rarity on the school children's feet (English and Gibson, 1959).

The two potential reservoirs of infection in swimming-baths are the pool itself and the surrounding floors. Infection could be by fragments of skin in which the fungus is embedded, or direct by conidia and hyphae of the saprophytically growing fungus. There is no evidence that dermatophytes exist in a saprophytic condition in these baths, as brushing down effectively removes contamination. It is unlikely that fragments of skin floating in the pool could attach themselves firmly enough to the feet to start an infection, and Tritsmans and Vaubreuseghem (1955) were unable to isolate dermatophytes from swimming-baths by setting "baits" of hair in the water, a method which is successful for collecting keratophilous fungi in soil. It is probable, therefore, that the main source of infection is pieces of infected skin pressed on to the foot while walking over contaminated floors.

The frequency with which *T. mentagrophytes* was isolated from the boys' changing accommodation compared with that of the girls, which is in agreement with an incidence of tinea pedis four times greater in boys than in girls using these baths (English and Gibson, 1959), is evidence for the importance of swimming-baths as a source of infection with tinea pedis in children. Also, the greater contamination of bath A coincides with the high incidence of tinea pedis in district A, found in the same survey, and it is possible that both are attributable to the lack of sluicing down of this bath, as well as to the more extensive use made of their bath by schools in this district compared with other districts.

The implication here is of a vicious circle of foot infection and floor contamination. A highly infected population would shed more infective particles than a slightly infected one, and this in turn would increase the risk for hitherto healthy users. As cleaning methods appear to be effective, cross-infection must occur mainly between bathers using the baths between each cleaning. Almost continuous cleaning and sluicing, as is already done in some baths, would appear to be a practical way of preventing the accumulation of contaminating particles.

The high incidence of tinea pedis in those members of the staffs who enter the water compared with those who do not, also implicates the baths as a source of infection and suggests that a regular mycological examination of the feet of such people could be undertaken with advantage.

Though this investigation was not planned on a statistical basis the results do add further to the evidence of Amrein and of Tritsmans and Vanbreuseghem that swimming-baths are an important source of infection with tinea pedis.

Summary

Trichophyton mentagrophytes has been isolated repeatedly from the floors of three swimming-baths by Gentles's direct sampling technique.

The fungus was found more often in baths and parts of baths used by populations with a high incidence of tinea pedis than in those used by populations with a lower incidence.

Brushing down and frequent sluicing appear to be reasonably effective methods of removing infective particles.

Eight out of 14 members of the swimming-bath staff whose duties entailed their entering the water were found to be suffering from tinea pedis. None of the 11 persons who never swam were infected.

It is concluded that swimming-baths are an important source of infection with tinea pedis.

We are indebted to Mr. J. Hancock, chief superintendent of Bristol's swimming-baths, for his ready permission to carry out this investigation, and to Mr. J. McA. Milne, chief organizer of physical education in Bristol, and the superintendents and staffs of the baths for their co-operation. Our thanks are also due to Dr. R. P. Warin and Dr. C. D. Evans, of Bristol Royal Hospital, and to Dr. R. C. Wofinden, medical officer of health, Bristol, for their interest and encouragement.

REFERENCES

Ajello, L., and Getz, M. E. (1954). *J. invest. Derm.*, **22**, 17.
Amrein, H. P. (1953). *Praxis*, **42**, 197.
English, Mary P., and Gibson, Mary D. (1959). *Brit. med. J.*, **1**, 1442.
Gentles, J. C. (1956). *J. clin. Path.*, **9**, 374.
Tritsmans, E., and Vanbreuseghem, R. (1955). *Belg. T. Geneesk.*, **11**, 625.

HOW CHRONIC IS PULMONARY TUBERCULOSIS IN THE ELDERLY?

BY

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It is now generally recognized that pulmonary tuberculosis is increasingly becoming a disease of older people and particularly of men over the age of 65. The notification rate for pulmonary tuberculosis in men over this age in England and Wales has almost doubled in the sixteen years from 1938 to 1954 (Wilkins, 1956). Likewise in New York City the number of newly diagnosed cases in men over 45 years of age is twice that of a generation ago (Robins, 1953). This increase in the disease in older people is not accounted for merely because there is a higher percentage of elderly people in the population. In the 1957 Glasgow mass *x*-ray campaign, for example, the yield of active pulmonary tuberculosis was 7.0 per 1,000 examined in those over 60, compared with 4.37 per 1,000 examined in the age group 15–59 years (Glasgow Corporation, 1958).

Traditionally, pulmonary tuberculosis in older people is supposed often to masquerade for years as chronic bronchitis. From textbook to textbook the picture is painted of the elderly parent or grandparent, with "chronic bronchitis," disseminating infection among household and other contacts. Nash (1955), endorsing this view, has suggested that if men over 45 could be *x*-rayed once "it would drain the unknown infector pool of most of its long-term members."

On the other hand, the presenting features of many cases of pulmonary tuberculosis in the elderly seen at Ruchill Hospital suggested that the disease might be of recent origin, and it was thought that further investigation of the problem would be profitable. Accordingly in 100 consecutive cases of pulmonary tuberculosis newly diagnosed in people over 55 every

effort was made to obtain previous chest *x*-ray films and, failing these, radiological reports. These cases were unselected in regard to both type and extent of disease.

Results

Fifty patients had had their chests *x*-rayed, 12 of them more than once. Radiological reports of all these films were obtained, and in 33 cases the films were also available. In 23 (46%) of these 50 cases the chest had been reported as radiologically clear. In the remaining 27 (54%) an abnormality had been noted. In one further case the patient had been *x*-rayed because of a fractured arm, and the film showed early active pulmonary tuberculosis in the left apex which had been visualized incidentally: this tuberculous disease had not been reported. Six years later, at the age of 69, this woman was found to have gross tuberculous infiltration in the left lung, with a large upper-lobe cavity.

The available films were reassessed by me and an experienced chest radiologist. In the 23 cases originally reported as clear, apical fibrosis was noted in two cases; and in a further film two small calcified foci were seen in an upper lobe. These appearances were minimal, and the films might well have been passed as normal.

The abnormalities reported in the remaining 27 cases were inactive fibrotic tuberculosis (12), unresolved pneumonia (7), bronchitic changes (4), miliary opacities (1), bronchiectasis (1), calcified foci (1), and pleural effusion (1).

In all cases in which inactive tuberculosis had been originally reported there was agreement when the films were reassessed, except in one in which it was felt that the possibility of activity might have been raised and in another in which a small area of fibrosis in the contralateral side had been overlooked.

Seven patients, admitted to various hospitals with pneumonia, had been discharged before radiological resolution was complete. In two cases retrospective examination of the films showed that significant radiological features had been overlooked: in one case the development in serial films of a small area of infiltration in the contralateral lung, and in another the presence of a small pleural effusion.

In four cases a diagnosis of chronic bronchitis had been made presumably because of increased lung markings associated with some fibrosis and emphysematous change.

The possibility of miliary tuberculosis was reported in one patient, but the occupational history and subsequent progress confirmed a retrospective diagnosis of pneumoconiosis.

In two successive years left-lower-lobe bronchiectasis had been reported in a patient with a long history of cough, purulent spit, and dyspnoea; infiltration in both upper lobes had been overlooked. This was reported when a year later he was admitted to hospital with an acute exacerbation of his "bronchiectasis." Sputum examination, carried out apparently for the first time, revealed numerous tubercle bacilli.

Age at Previous X-ray Examination.—Table I shows the ages of the patients when the original plates had been taken. In only three cases was the patient under 50. The earliest age at which a previous film had been carried out was 42; this film was clear. Thus out of 50 cases no fewer than 47 were 50 years of age or over when first *x*-rayed. Further, 15 patients had been

TABLE I

Result of Original *X*-ray Examination	Age (in Years) at Previous *X*-ray Examination					Total
	–49	49–54	55–59	60–64	65+	
Clear	1	10	5	5	2	23
Abnormal ..	2	5	10	5	5	27
Total ..	3	15	15	10	7	50

x-rayed when 55 to 59 years old, and in five the films were clear; 10 had been *x*-rayed at ages 60 to 64 years, and in five the films were clear; finally seven had been originally *x*-rayed when aged 65 or more, two of these *x*-ray films being reported clear.

Duration Between Diagnosis of Tuberculosis and Previous X-ray Examination.—Table II shows the length of time elapsing between diagnosis and the previous films. Only 12 of the 50 patients were *x*-rayed more than five years prior to diagnosis, six with clear films

TABLE II

Result of Original *X*-ray Examination	Length of Time (in Years) Since Previous *X*-ray Examination										Total
	1	2	3	4	5	6	7	8	9	10+	
Clear	—	4	3	7	3	1	1	1	1	2	23
Abnormal ..	5	5	5	1	5	2	—	—	1	3	27
Total ..	5	9	8	8	8	3	1	1	2	5	50

and six having films in which an abnormality had been found. Thus 76% of the patients had been *x*-rayed within five years of diagnosis. In one patient a further *x*-ray examination of the chest, carried out only two months after a clear film, showed active tuberculosis at one apex.

Reason for Pre-diagnostic X-ray Examination

Previous *x*-ray examinations had been carried out for a variety of reasons: in 27 cases because of respiratory symptoms; in 13 during an investigation of non-respiratory illnesses; in 5 at mass radiography; in 3 because of contact with a known case of tuberculosis; and in 2 because of trauma (injury to thoracic cage).

Two points call for special comment. First, in two cases the evidence suggested that the disease had developed in the same manner as a primary tuberculous lesion. One patient aged 56 was first *x*-rayed two months before his daughter was diagnosed as having active pulmonary tuberculosis. His *x*-ray film was then clear. Two years later he developed a left pleural effusion which resolved completely in six weeks. As there was no evidence of a tuberculous focus in the lung, it had apparently been concluded that the aetiology of the effusion was not tuberculous. However, after a further two years two new cases of active pulmonary tuberculosis presented in the household, and a further *x*-ray film of the parent's chest then showed active tuberculosis in the left mid-zone and right apex. Sputum contained tubercle bacilli. Another man developed a right pleural effusion at the age of 59, but, as it resolved quickly and he was found to have electrocardiographic changes suggestive of myocardial degeneration, the effusion was attributed to heart failure. A year later, however, he was *x*-rayed again because of dyspnoea, and infiltration in the right upper lobe was discovered. Examination of the sputum revealed tubercle bacilli.

The second point is that three patients, aged 55, 55, and 59 years at diagnosis, appear to have contracted the

disease as a result of infection from a younger member of the household. These patients had had a negative *x*-ray report after the source case had been diagnosed. In a further case, a man aged 51 whose wife had active tuberculosis had a clear *x*-ray film, but four years later he had developed bilateral pulmonary tuberculosis with cavitation.

Discussion

The aim of tuberculosis work is not now concerned so much with control of disease as with eradication of infection. Simmonds (1953) has pointed out that "as tuberculosis becomes less widespread its significance as an infectious disease tends to increase. The seed becomes relatively more important when it may find so many susceptibles." It is therefore of vital importance that the pool of unknown infected persons should be drained. Once diagnosed, practically all these cases, except the recalcitrant and unteachable, would soon cease to be public-health problems. Wilkins (1956) has shown that a large number of cases of pulmonary tuberculosis are to be found, especially in men over the age of 65, and recent trends in tuberculosis mortality and morbidity suggest that sources of active infection will be increasingly concentrated in this group.

It has generally been thought that tuberculosis in older people is a very chronic disease, and for this reason it has been suggested that a complete *x*-ray survey of men over 45 would be virtually sufficient to root out most of the disease in this group (Nash, 1955). The present investigation, however, suggests that this statement needs qualification.

It seems evident that some older people have a clear *x*-ray report and subsequently develop active tuberculosis. In this series of 100 people diagnosed as having pulmonary tuberculosis over the age of 55 years, 49 had had a previous chest *x*-ray examination when they were more than 45 years old. The original film of 22 (44.9%) of these 49 patients showed no evidence of intrapulmonary disease and many of them had been *x*-rayed within five years of diagnosis. Similarly, Wraith and Ovens (1956) found that, of 106 patients over the age of 50, 14 had had an apparently normal *x*-ray film taken within 10 years of the diagnosis of tuberculosis and in a further 11 cases *x*-ray films taken within a similar period showed only a slight amount of inactive tuberculous disease at one or both apices. It therefore seems that a negative *x*-ray report in an older person is of limited value only.

It is also evident from this investigation that further problems arise even if disease is noted. Tuberculous disease which appears radiologically inactive may break down, often after many years, and there are practical difficulties in arranging indefinitely prolonged observation. Also, radiological reports of bronchitic changes in the lungs of older people must be regarded with reserve; sputum examination for tubercle bacilli is desirable in all these cases. "Unresolved" pneumonias should, of course, be regarded with the greatest suspicion from the point of view of both tuberculosis and lung cancer, and, although the importance of observing such cases until radiological resolution or stability has been reached is well recognized, this series shows that action does not always follow upon knowledge.

Springett (1951) has found in mass radiographic studies that many new cases in older people are due to breakdowns of old lesions regarded as inactive at previous *x*-ray examinations, and no doubt in some cases the disease is due to reactivation of a lesion not radiologically visible. Medlar (1955) believes that in some cases, particularly in older men, the disease may arise as a result of exogenous infection, and there was evidence in the present investigation to support his contention. In four older patients it seems that the source of infection was an active case in the household. When the source case was diagnosed the elderly parent was radiologically free from infection. Further, in three of these cases, contrary to the usual course of events, the younger member of the household appeared to have infected the older. As eradication of tuberculous infection from the community proceeds such instances should become rarer.

Why should a person who has successfully resisted disease throughout adult life suddenly develop active pulmonary tuberculosis? It may be that disease in the older patients is facilitated by a waning of resistance to the tubercle bacillus (Pagel and Woolf, 1949; Lees and Munro, 1954). If previous tuberculous disease has healed completely any further infection occurs in what can be regarded as virgin soil. In such a case disease would be expected to assume the form of primary tuberculosis, and this in fact did happen in two cases.

How can these cases of active tuberculosis in older people best be detected? Obviously, regular mass surveys of older age groups would be the ideal method, but this is a counsel of perfection. The elderly are notoriously difficult to persuade to come for *x*-ray examination, and in the 1957 Glasgow mass *x*-ray campaign, despite intensive propaganda directed especially to the elderly, only 60.64% of men resident in the city over the age of 60 years came forward, compared with 76.24% of men in the age group 15–59. Similarly, 63.68% of women over the age of 60 were *x*-rayed, compared with 80.73% of those between the ages of 15 and 59.

It seems probable that the key figure in the attack against tuberculosis will be the general practitioner. The family doctor knows the patient, is most in contact with him professionally, and is in a good position to persuade him to submit to further investigation when he is ill. It must not be forgotten that, while in some old people pulmonary tuberculosis may present in an acute form, in others the onset may be much more insidious. Lassitude and loss of weight, too often regarded as a normal accompaniment of ageing, may be the only symptoms. Pyrexia and anaemia are uncommon, and a cough may be attributed to "bronchitis" or cigarettes. The disease progresses steadily, with no dramatic signs, and it is only after the patient has been under treatment for some time, with consequent marked improvement in his general condition, that he realizes by comparison how ill he was prior to diagnosis.

These deviations from the normal ageing process are most likely to be detected by the family physician. But, even though no respiratory symptoms or signs are present, the patient may have pulmonary tuberculosis, and the practitioner should not be deterred from having *x*-ray examination of the chest carried out because of a previous negative film, no matter how recent that may be. The necessity for re-examination of the chest is even more urgent if any abnormality has been previously detected. Lesions regarded as inactive may have reactivated, and changes in the lung fields thought to be due to bronchitis may have had a tuberculous basis.

Summary

The previous radiological history of 100 consecutive cases of pulmonary tuberculosis in which the patient was over the age of 55 years was investigated.

Fifty had been *x*-rayed before: 23 (46%) of these films were clear and 27 (54%) showed no abnormality.

In films considered abnormal, inactive tuberculosis, "unresolved pneumonia," and "bronchitic changes" were the most common abnormalities found.

Only three patients were under the age of 50 when previously *x*-rayed, and 38 patients had been *x*-rayed within five years of diagnosis.

In an older person if any suspicion of pulmonary tuberculosis arises it is essential to carry out an *x*-ray examination of the chest even if a recent film has been reported clear.

I wish to thank Dr. A. W. Lees, consultant chest physician, Ruchill Hospital, for his constant interest in this investigation, and Dr. Agnes Macgregor for her assessment of the radiographs.

REFERENCES

Glasgow Corporation (1958). *Glasgow's X-ray Campaign Against Tuberculosis, 1957.*
Lees, A. W., and Munro, I. B. (1954). *Brit. med. J.*, **1**, 496.
Medlar, E. M. (1955). *Amer. Rev. Tuberc.*, **71**, Suppl. [No. 3, Pt. 2], p. 220.
Nash, F. A. (1955). *Lancet*, **2**, 1302.
Pagel, W., and Woolf, A. L. (1949). *Amer. Rev. Tuberc.*, **59**, 311.
Robins, A. B. (1953). *Amer. J. publ. Hlth*, **43**, 718.
Simmonds, F. A. H. (1953). *Tubercle (Lond.)*, **34**, 314.
Springett, V. H. (1951). *Brit. med. J.*, **2**, 144.
Wilkins, E. G. (1956). Ibid., **1**, 883.
Wraith, D. G., and Ovens, R. (1956). *Brit. J. Tuberc.*, **50**, 326.

IDIOPATHIC HYPOPARATHYROIDISM WITH NORMAL URINARY CALCIUM

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The association of symmetrical calcification of the basal ganglia with hypoparathyroidism was reported by Eaton and Haines (1939), and is now well recognized. In these cases, low levels of serum calcium accompany high levels of serum phosphate, in the absence of any evidence of renal insufficiency, generalized bone disease, or abnormality of fat absorption. Calcium is absent from the urine; indeed, its reappearance there is the yardstick of treatment recommended by Albright and Reifenstein (1948). These authors further note, however, the rare occurrence of cases in which calcium in normal quantities was present in the urine. Such a case is here recorded.

Case Report

The patient, a man aged 21, was resident in North-west Scotland and came of a family of four, with two sisters aged 25 and 8 years, and one brother aged 15 years. None save the patient gave any history of epilepsy or other neurological or endocrine disease. Radiographs of the skull of his brother and younger sister were normal. His father, aged 55, and mother, aged 48, were in good health and gave no history of neurological or endocrine disease, and their skull radiographs showed nothing abnormal. His father's two brothers, aged 61 and 50, and his mother's three brothers, aged 58, 50, and 44, were all reported to be in good health. They and the patient's elder sister were either abroad or in inaccessible parts of Northern Scotland. Radiographs of these relatives were not obtained. The patient himself had suffered from recurrent convulsions at the age of a few weeks, attributed to birth trauma. Throughout his childhood, up to the age of 8 years, he had occasional epileptiform seizures. Thereafter he had suffered from such seizures only in response to febrile illness. There had been two such occasions in adolescence, while his first admission to another hospital and transfer to Aberdeen (December, 1957) had resulted from such a convulsion occurring in the course of influenza. For long he had been thought to be suffering from idiopathic epilepsy.

There was nothing to suggest deterioration in his general health or intellectual capacity. His memory was good, his mother had noticed no change in his personality, and he was working successfully as a stone-mason.

Examination revealed a co-operative, pleasant young man, rather slow in conversation though his speech was normal. He was easily amused, and other patients found him odd or simple without clear foundation for their opinions. Assessment of intelligence on the Wechsler adult scale gave an intelligence quotient of 90. He seemed of at least dull average intelligence, while his memory and reasoning ability appeared to be normal.

Bilateral lens opacities were detected by slit-lamp examination. The optic fundi were normal. Bilateral horizontal nystagmus was more pronounced to the right. There was no tremor of the limbs, but fine tremor of the tongue and of the eyelids on closure was constantly present. No jaw-jerk was elicited. Normal tone was present in arm and leg muscles. His performance of fine repetitive hand movements appeared to be slightly impaired.

Romberg's sign was negative. Though his gait was brisk he swung his arms considerably less than normal. He admitted no paraesthetic phenomena, nor were any abnormalities of sensation detected.

The Chvostek and Trousseau signs were initially negative, but after several days in hospital, with a much reduced milk intake as compared with his home diet, these signs became unequivocally positive, although no apparent change in the serum levels of calcium and phosphate had occurred. Trousseau's sign was elicited as recommended by Albright and Reifenstein (1948), an arm tourniquet being elevated to just above the systolic blood pressure for three minutes. Erb's test, invoked because of initially negative clinical tests, gave a cathodal opening contraction at 4.5 mA.

General examination revealed no abnormality; blood pressure was 120/70. The teeth generally were of poor development, very carious, with much gum infection. The nails and hair appeared normal, and the skin was of average texture.

Investigations

Radiographs of the skull (Figs. 1–3) showed extensive irregular calcification in the basal ganglia of both sides and calcification in both dentate nuclei. There was also some hyperostosis of the frontal and parietal bones. The long bones, hands, chest, and abdomen showed no radiological abnormality. There was no subcutaneous or renal calcinosis. Radiographs of the teeth confirmed their poor development. Many of them were mere stumps with evidence of apical infection. The lower incisors had particularly small roots (Figs. 4–6). The trabeculae of the lumbar spine were noticed to be prominent, but there was no evidence of generalized increase in bone density. On admission the serum calcium was 6.2 mg./100 ml. and the serum phosphate 6.1 mg./100 ml. Serum acid and alkaline phosphatases were found to be 1.5 and 10 King–Armstrong units respectively. Total serum protein was 8.3 g./100 ml. (albumin/globulin ratio 1.6/1). The blood urea was 37 mg./100 ml., and plasma CO_2 combining power 66 vols./100 ml.

FIG. 1

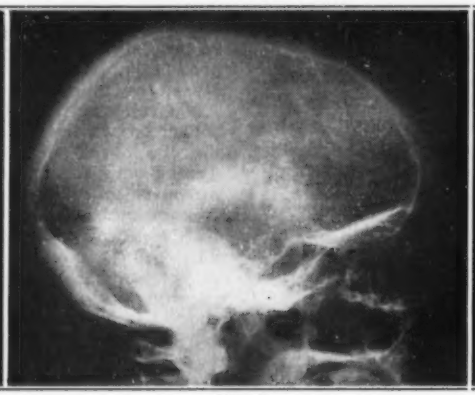

FIG. 2

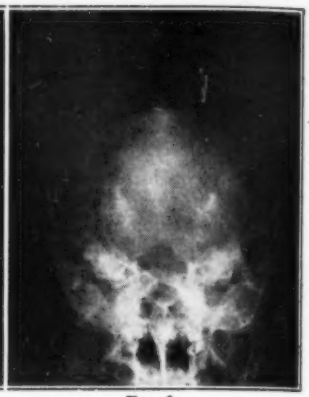

FIG. 3

FIGS. 1-3.—Radiographs of the skull—antero-posterior, lateral, and Townes's view—showing calcification.

FIG. 4

FIG. 5

FIG. 6

FIGS. 4-6.—Lower incisors, upper molars, and upper incisors, showing poor development and extensive caries.

Examination of the C.S.F. revealed normal dynamics, with a protein content of 20 mg./100 ml., and one lymphocyte per c.mm. W.R. on blood and C.S.F. was negative. The complement-fixation test for toxoplasmosis was negative. The electroencephalogram showed no notable abnormality.

The urine contained no sugar or albumin and the urea clearance (standard) was 82% of normal. No excess amino-acids were present, the pattern of excretion being normal. The urinary excretion of calcium on a normal hospital diet was found to be 300 mg. a day, the urinary phosphate excretion 1.25 g. a day.

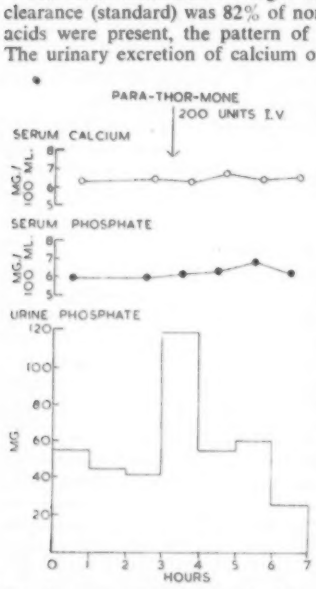

FIG. 7.—Ellsworth-Howard test. The effect of para-thor-mone administered intravenously on the urinary phosphate excretion.

After five days' acclimatization on a low dietary calcium intake (0.2 g. a day), the total calcium excretion was measured over three consecutive three-day periods. The total daily excretion of calcium averaged 263 mg.—160 mg. in the urine and 103 mg. in the faeces. This gave a negative calcium balance of 63 mg. a day.

The Ellsworth-Howard test was performed as described by Albright and Reifenstein (1948). 200 *U.S.P.* units of fresh "para-thor-mone" was injected intravenously, with hourly urine collection by indwelling catheter for two hours before and four hours after injection. A roughly threefold increase in phosphate excretion was noted (Fig. 7).

A calcium infusion test was performed after the method of Nordin and Fraser (1954). The rise in serum phosphate associated with a rise in both urinary phosphate output and renal phosphate/creatinine clearance ratio (Fig. 8) falls into the pattern described by Nordin and Fraser (1956) in cases of hypoparathyroidism.

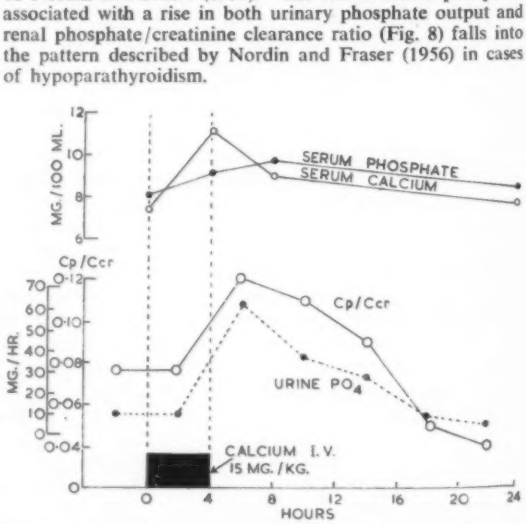

FIG. 8.—Changes in serum calcium and phosphate, urinary phosphate excretion, and renal phosphate/creatinine clearance rates after intravenous calcium infusion (15 mg./kg. body weight).

$$C_p/C_{cr} = \frac{\text{Urinary phosphate} \times \text{serum creatinine}}{\text{Urinary creatinine} \times \text{serum phosphate}}$$

(Owing to initial difficulty in emptying the bladder, the first two results here are mean values.)

Treatment with Dihydrotachysterol and Calciferol

Dihydrotachysterol (A.T. 10) and calciferol are generally regarded as of equal efficacy in the treatment of hypoparathyroidism and pseudohypoparathyroidism (McLean, 1941). Several reports in the literature (Blohm *et al.*, 1953; MacGregor and Whitehead, 1954) indicate the occasional failure of dihydrotachysterol to elevate the serum calcium. In this case we found no response to a nine-days trial of dihydrotachysterol, although admittedly small doses were employed (Fig. 9).

As the patient lived some two days' journey from the hospital the follow-up was entirely dependent upon the good offices of the local practitioner, who kindly arranged to transmit a sample of whole blood to us weekly. Once a month a 24-hour collection of urine in "polythene" bottles, to which 10 ml. of concentrated hydrochloric acid had been added, was also sent to the laboratory. Every three months the patient himself visited hospital for a few days' check-up.

Elevation of the serum calcium required much larger doses of calciferol than we had envisaged, a daily intake of 250,000 units being reached by stages before any perceptible rise took place. On this dose, however, fairly rapid elevation of his serum calcium level occurred (Fig. 9). Reduction of the dosage to 100,000 units a day was followed by a rapid fall in serum calcium; recovery was steady with a return to a higher dosage (200,000 units a day).

The routine estimation of phosphate levels was also performed on these sera, but occasional gross haemolysis vitiated several of the results, and reliance was placed upon the calcium level in the serum as a therapeutic guide.

The effect of calciferol upon the 24-hour excretion of calcium and phosphorus is shown in Fig. 9. When his serum calcium was in the normal range on a calciferol dosage of 250,000 units a day, a 24-hour sample of his urine (volume 1,740 ml.) contained 1,455 mg. of calcium. This extremely high calcium excretion contributed to our decision to cut the calciferol dosage drastically at this point. It is clear, however, that there is little variation in the daily excretion of phosphate as the serum level fluctuates. At the time when his serum calcium reached normal levels and his urinary calcium output was very high, his phosphate output was 1.04 g. per 24 hours. We took this to indicate continuing satisfactory renal function.

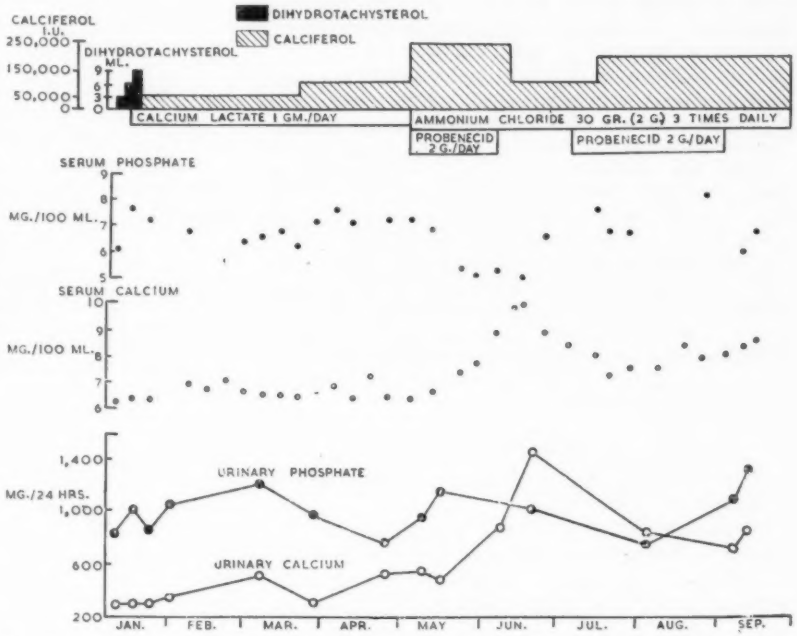

FIG. 9.—Effect of dihydrotachysterol and calciferol on serum calcium and phosphate, and on urinary calcium and phosphate excretion.

Dietary Measures

Albright and Reifenstein (1948) recommend the addition of a calcium salt to the diet, and for the first few months of treatment the patient took 1 g. of calcium as calcium lactate in addition to a normal diet. He was asked to reduce his previous milk intake of about 2 pints (1,140 ml.) a day to about ½ pint (280 ml.). This meant his complete abandonment of milk as a beverage. At the time of his second admission to hospital (May, 1958), however, his calcium lactate was discontinued. This salt contains such a small proportion of calcium that the large number of tablets necessary to provide an added gramme of calcium constitutes a real therapeutic difficulty.

From May, 1958, ammonium chloride, 30 gr. (2 g.) three times daily, was added to the diet. This has been supposed (Lachmann, 1941) to increase the ionization of serum calcium, but its use in our case was prompted mainly by the desire to ensure the production of an acid urine in view of the high level of calcium excretion with attendant dangers of stone formation.

Albright and Ellsworth's (1929) view of the mode of action of para-thor-mone would suggest that a phosphate diuresis, however produced, might aid the elevation of serum calcium levels. The use of probenecid ("benemid") was suggested to us by Nordin (1958, personal communication). This substance, besides increasing the urinary output of uric acid, has also been observed to increase the excretion of phosphate. Our data provide no confirmation of this. The withdrawal of probenecid while the patient was on high calciferol dosage, and its recommencement at much lower serum calcium levels on a lower dose of calciferol, did not affect the trend of the serum response at all (Fig. 9). We were unable to demonstrate the disappearance of the clinical signs of tetany with the return of the serum calcium to normal in June, as the patient was not at that time in hospital; but on his admission in September, when the serum calcium level was 8.3 mg./100 ml., both the Chvostek and the Trousseau signs were negative. The calcification in his basal ganglia was at this time unchanged. His neurological signs had not advanced, nor had his lens opacities increased.

Discussion

The biochemical and radiological findings in this case of epilepsy are together sufficient to support the diagnosis of hypoparathyroidism. The absence of stigmata of the peculiar syndrome of pseudohypoparathyroidism, short metacarpal bones, stunted stature, and soft-tissue calcification, together with the clinical history, and convulsive episodes dating from early childhood, are sufficient to justify a diagnosis of idiopathic hypoparathyroidism. The response to para-thor-mone shown by the Ellsworth-Howard test may be taken as further

evidence in this differentiation, although the usefulness of this test has been disputed (Milne, 1951 ; Dent, 1953 ; MacGregor and Whitehead, 1954).

Of great interest, however, is the finding in our case of normal or high levels of calcium excretion in the urine. Reviews of published cases of idiopathic hypoparathyroidism (Lachmann, 1941 ; Steinberg and Waldron, 1952) are reticent on the matter of urinary calcium content. The records of most cases contain bare statements that the Sulkowitch test was either "negative" or "faintly positive"—findings which, according to Albright and Reifenstein (1948), indicate blood calcium levels of "below 7.5 mg. per 100 ml." They further admit, however, that certain individuals apparently have a low renal threshold for calcium excretion, and mention, without further details, three patients with hypoparathyroidism who excreted large amounts of calcium in the urine at low levels of serum calcium.

It would appear preferable, where possible, in further studies of cases of hypoparathyroidism to substitute for the Sulkowitch test the more precise assay of daily calcium excretion. It does not seem to us adequate to regulate the calciferol dosage by the Sulkowitch test without periodic checks upon the serum calcium level. In our own case the absence of other urinary abnormality, together with the increase in urinary calcium excretion parallel with elevation of the serum calcium, suggests an abnormality of renal threshold for calcium, an "idiopathic hypercalciuria." There is no evidence of osteoporosis, and the radiological abnormalities typical of hypoparathyroidism suggest that the hypercalciuria is no more than an incidental unassociated abnormality.

Summary

A case of idiopathic hypoparathyroidism presenting with epilepsy is described.

Restoration of normal serum levels of calcium and phosphate was achieved with calciferol in high dosage.

The unusual finding of a high normal daily calcium excretion in the urine before treatment is discussed.

Our thanks are due to Mr. W. M. Nichols for permission to publish this case and for his continued encouragement, to Dr. M. MacLeod for his advice and criticism, and to Mr. Topp for the photographs. We are particularly indebted to Dr. F. A. Macrae, Kyle of Lochalsh, for his unfailing help in the follow-up of the case.

REFERENCES

Albright, F., and Ellsworth, R. (1929). *J. clin. Invest.*, **7**, 183.
—— and Reifenstein, E. C. (1948). *The Parathyroid Glands and Metabolic Bone Disease*. Williams and Wilkins, Baltimore.
Blohm, R. W., Wurl, O. A., Gillespie, J. O., and Escamilla, R. F. (1953). *J. clin. Endocr.*, **13**, 519.
Dent, C. E. (1953). *Proc. roy. Soc. Med.*, **46**, 291.
Eaton, L. M., and Haines, S. F. (1939). *Proc. Mayo Clin.*, **14**, 48.
Lachmann, A. (1941). *Acta med. scand.*, Suppl. 121.
MacGregor, M. E., and Whitehead, T. P. (1954). *Arch. Dis. Childh.*, **29**, 398.
McLean, F. C. (1941). *J. Amer. med. Ass.*, **117**, 609.
Milne, M. D (1951). *Clin. Sci.*, **10**, 471.
Nordin, B. E. C., and Fraser, R. (1954). Ibid., **13**, 477.
—— —— (1956). In *Ciba Foundation Symposium on Bone Structure and Metabolism*, p. 222. Churchill, London.
Steinberg, H., and Waldron, B. R. (1952). *Medicine (Baltimore)*, **31**, 133.

The Medical Directory for 1959, the 115th annual issue, is now available from Messrs. J. & A. Churchill Ltd., 104 Gloucester Place, London, W.1 (2 parts ; 4 guineas). It contains 91,206 names, an increase of nearly 2,000 over the previous issue.

SERUM HAPTOGLOBINS IN HEPATOBILIARY DISEASE

BY

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Haptoglobins are globulins which combine with haemoglobin (Polonovski and Jayle, 1940). We have measured serum haptoglobins in 64 patients with hepatobiliary disease and have found that levels are low in parenchymatous liver disease and high in biliary obstruction. We have assessed the measurement of serum haptoglobins as an index of hepatic function in hepatitis and cirrhosis, and as an aid in the differential diagnosis of the jaundiced patient.

Material and Methods

A range of normal values was obtained by analysing sera from 50 healthy blood donors. The 64 patients with hepatobiliary disease were classified as follows: (1) Acute infective hepatitis. (2) Active chronic hepatitis: hepatitis and cirrhosis of uncertain aetiology, including cases of post-hepatitic and post-necrotic cirrhosis. (3) Lupoid hepatitis: active chronic hepatitis and a positive L.E. cell test (Mackay *et al.*, 1956). (4) Nutritional cirrhosis (Laennec's cirrhosis, alcoholic cirrhosis): all patients in this group admitted to a high intake of alcohol. (5) Extrahepatic biliary obstruction due to gallstones, neoplasm of the biliary tract or pancreas, or, surgical damage to the common bile duct. None of these patients had biliary cirrhosis. (6) Miscellaneous (see Table I).

Serum haptoglobins were measured by determining the amount of haemoglobin which must be added to serum to saturate the haptoglobins present. Haemoglobin solutions of different concentrations were prepared from washed human erythrocytes lysed with water. 0.1 ml. of each solution was added to 0.2 ml. of the serum to be analysed, giving serum haemoglobin concentrations varying from 0 to 400 mg. per 100 ml. The mixtures were analysed by paper electrophoresis (phosphate buffer 0.025 M, *p*H 6.5, temperature 3–5° C., potential gradient 10 v. per cm., duration four hours). Under these conditions the haemoglobin-haptoglobin complex migrates towards the anode while haemoglobin remains at the origin. After electrophoresis the strips were stained with a dianisidine reagent (Owen *et al.*, 1958) and the minimal amount of added haemoglobin which produced a zone of free haemoglobin was noted. Results, in mg. of bound haemoglobin per 100 ml. of serum, were expressed as the range between the amount of added haemoglobin which just failed to produce a zone of free haemoglobin on the paper strip and the amount which was just sufficient for this (Fig. 1).

*Working with the aid of a grant from the National Health and Medical Research Council of Australia.

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Serum glutamic oxalacetic transaminase was determined by the method of Reitman and Frankel (1957), serum albumin was separated as described by Hawk *et al.* (1937) and measured by the biuret method of Gornall *et al.* (1949), and the serum bilirubin method was that of Malloy and Evelyn (1937).

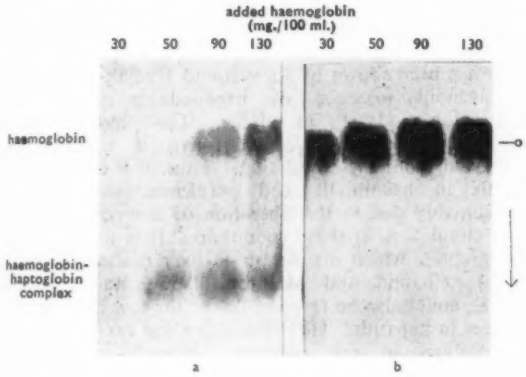

FIG. 1.—Electrophoretic determination of haptoglobins (strips stained with dianisidine reagent). O indicates the origin; the arrow indicates direction of migration. Haptoglobin values: (*a*) 50–90 mg. per 100 ml.; (*b*) 0–30 mg. per 100 ml. In strip (*a*) 90 mg. per 100 ml. of added haemoglobin has saturated the serum haptoglobin as shown by the presence of free haemoglobin. In strip (*b*) 30 mg. per 100 ml. of added haemoglobin was sufficient for this.

Results

Results of haptoglobin determinations for all subjects are shown in Table I. The mean value in the normal subjects was 84 mg. per 100 ml., which agrees with that obtained by Laurell and Nyman (1957) using a similar method, and with that obtained by Jayle and Boussier (1955) and by Nyman (1958a) using a method based on the peroxidase activity of the haemoglobin-haptoglobin complex.

TABLE I.—*Serum Haptoglobin Levels in Normal Subjects and in Hepatobiliary Disease*

Condition	Total No. of Cases	Case Distribution for Different Ranges of Serum Haptoglobin Level (as Haemoglobin in mg./100 ml.). (Figures Indicate Number of Patients)							Mean Haptoglobin Level
		0–15	15–30	30–50	50–90	90–130	130–200	200 ^	
Normal subjects	50	—	—	7	20	19	4	—	84
Acute infective hepatitis ..	5	—	2	1	2	—	—	—	45
Active chronic ,, ..	16	5	3	2	3	1	2	—	42
Lupoid hepatitis	10	5	2	1	2	—	—	—	26
Nutritional cirrhosis	13	2	1	3	2	5	—	—	65
Extrahepatic biliary obstruction	12	—	—	—	1	3	4	4*	185
Miscellaneous:									
Metastatic carcinoma of liver	2	—	—	—	—	—	2	—	—
Primary biliary cirrhosis ..	1	—	—	—	—	1	—	—	—
Obstructive ,, ,, ..	2	—	2	—	—	—	—	—	—
Indeterminate cirrhosis ..	1	—	—	—	1	—	—	—	—
Obstructive hepatic necrosis	1	1	—	—	—	—	—	—	—
Haemochromatosis	1	—	—	1	—	—	—	—	—

* Values were, respectively, 200–250, 300–400, 300–400, and 400–500 mg. 100 ml.

Acute Infective Hepatitis.—In the five patients, serum haptoglobin levels were either low-normal or low.

Active Chronic Hepatitis and Lupoid Hepatitis.—Of 26 cases studied, 18 had serum haptoglobins in the range of 0–50 mg. per 100 ml., and 15 had values below 30 mg. per 100 ml. In the few cases having haptoglobin values within the normal range, liver function was good, whereas low values were obtained in patients with more severe liver involvement. Four critically ill patients in this group had no demonstrable serum haptoglobins.

Nutritional Cirrhosis.—Of 13 cases, three had low levels (<30 mg. per 100 ml.) whilst the remainder had normal levels.

Extrahepatic Biliary Obstruction.—In this group haptoglobin levels were either normal or high; four patients had considerably elevated levels (Table I, footnote).

Miscellaneous.—In two patients with metastatic carcinomatosis of the liver, haptoglobin values were high-normal; in two patients with obstructive biliary cirrhosis values were low. Haptoglobin values in other liver conditions are presented in Table I.

In certain patients with chronic hepatitis, serum haptoglobins have been measured at intervals; the results (Table II) indicate that changes in serum haptoglobin level tended to parallel changes in clinical status.

TABLE II.—*Serial Serum Haptoglobin Levels in Liver Disease*

Case	Diagnosis*	Period of Observation (Months)	Haptoglobin Level (as Hb in mg./100 ml.)	Clinical Course
DEL	LH	0 7	0–15 50–70	Improved with cortisone
EGL	ACH	0 10	0–15 90–130	,, ,,
MAG	LH	0 9 11	50–70 110–150 130–150	,, ,,
TIN	LH	0	50–90 90–130	,, ,,
BUG	NC	0 4	15–30 0–15	No response to medical treatment, including prednisolone
SAV	ACH	0 12	0–15 0–15	Compensated cirrhosis; no change
GRL	NC	0 1	30–50 0	Deterioration

* LH = Lupoid hepatitis. ACH = Active chronic hepatitis. NC = Nutritional cirrhosis.

In 32 patients (excluding the miscellaneous group) jaundice was present (serum bilirubin >2 mg. per 100 ml.). In 14 of these jaundice was due to acute infective hepatitis, active chronic hepatitis, or lupoid hepatitis; the mean haptoglobin level in this group was 35 mg. per 100 ml., and all but one had values below 90 mg. per 100 ml. (Table III). Jaundice was due to biliary obstruction in 12 cases; the mean haptoglobin level in this group was 185 mg. per 100 ml., and all but one had values above 90 mg. per 100 ml. In cases of nutritional cirrhosis with jaundice, values were intermediate.

In certain patients with hepatitis and cirrhosis the serum haptoglobin level was compared with the serum

TABLE III.—*Distribution of Serum Haptoglobin Levels in 32 Patients with Jaundice*

Condition	Total No. of Cases	Case Distribution for Different Ranges of Serum Haptoglobin Level (as Hb in mg./100 ml.)			
		0–50	50–90	90–130	>130
Acute infective hepatitis, active chronic hepatitis, lupoid hepatitis	14	8	5	–	1
Extrahepatic biliary obstruction	12	–	1	3	8
Nutritional cirrhosis	6	2	–	4	–

albumin level (Fig. 2), and with the level of serum glutamic oxalacetic transaminase (Fig. 3). The data suggest that low haptoglobin levels were associated with advanced parenchymal damage as indicated by low serum albumin levels (Fig. 2), and in a less consistent manner with active necrosis of the liver, as indicated by high transaminase values (Fig. 3).

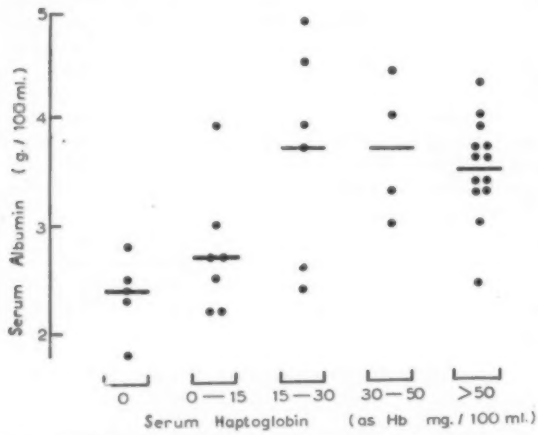

FIG. 2.—Comparison of serum albumin level with serum haptoglobin level. Horizontal lines indicate mean values for each group. Low serum albumin levels are associated with low levels of serum haptoglobin.

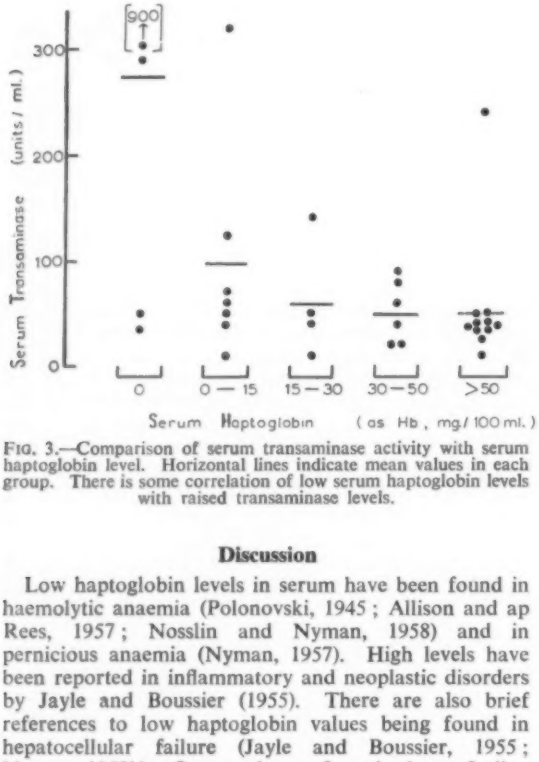

FIG. 3.—Comparison of serum transaminase activity with serum haptoglobin level. Horizontal lines indicate mean values in each group. There is some correlation of low serum haptoglobin levels with raised transaminase levels.

Discussion

Low haptoglobin levels in serum have been found in haemolytic anaemia (Polonovski, 1945; Allison and ap Rees, 1957; Nosslin and Nyman, 1958) and in pernicious anaemia (Nyman, 1957). High levels have been reported in inflammatory and neoplastic disorders by Jayle and Boussier (1955). There are also brief references to low haptoglobin values being found in hepatocellular failure (Jayle and Boussier, 1955; Nyman, 1958b). Our results confirm the latter finding and further indicate that determination of serum haptoglobins may be of value in the following clinical situations: firstly, in assessing the degree and progress of hepatocellular damage in patients with hepatitis and cirrhosis; and, secondly, in the differential diagnosis of jaundice, wherein low levels suggest parenchymal damage and high levels suggest biliary obstruction. Nutritional cirrhosis was less often associated with low haptoglobin values than was active chronic hepatitis or lupoid hepatitis, and this corresponds with our experience that there is less disturbance of liver function in nutritional cirrhosis than in the latter conditions (Wood, 1959).

It has been shown by Laurell and Nyman (1957) that intravenous injection of haemoglobin causes the haptoglobin level to fall. The haemoglobin–haptoglobin complex which forms is subsequently removed from the circulation. Thus, low haptoglobin levels in haemolytic and pernicious anaemia are presumably due to the liberation of haemoglobin into the circulation in these conditions. It is possible that haemolysis, which may occur in liver disease (Watson, 1939; Chaplin and Mollison, 1953; Raffensperger, 1958), could also be responsible for the low haptoglobin values in hepatitis. However, there was no evidence of haemolysis in our patients, although cell-survival studies were not done.

It should be noted that with the method used any haemoglobin already present in the serum as a result of *in vitro* haemolysis reduces the result. However, this was not the cause of the low values found in hepatocellular disease, since sera with visible haemolysis were not analysed, whilst doubtful specimens were analysed without the addition of haemoglobin and those containing appreciable amounts of haemoglobin were discarded.

Smithies (1955) has shown that persons can be divided into three distinct groups on the basis of the electrophoretic haptoglobin pattern, and Nyman (1958a) has reported that mean haptoglobin values in normal persons depend somewhat on the haptoglobin type. We did not take into account the haptoglobin type of our patients, since determination of this requires starch-gel electrophoresis, which is not, as yet, a procedure suitable for the average hospital laboratory. We do not think, however, that this omission has seriously influenced our assessment of serum haptoglobin analysis.

We believe that low haptoglobin levels in liver disease are the result of hepatocellular failure. Low levels of plasma albumin in liver disease have been attributed directly to a reduced capacity of the damaged liver to synthesize albumin, and this may also apply to haptoglobins. At present we can offer no explanation for the abnormally high values found in patients with obstructive jaundice.

Summary

Serum haptoglobins have been estimated by a simple paper electrophoretic method in 50 normal persons and in 64 patients with hepatobiliary disease.

Haptoglobin values were low in hepatocellular failure and high in biliary obstruction and secondary carcinomatosis.

Measurement of the serum haptoglobin level is of value in assessing the degree of hepatocellular damage.

The test is useful in the differential diagnosis of jaundice.

Members of the honorary medical staff of the Royal Melbourne Hospital kindly permitted access to their cases.

We are indebted to Dr. Sara Weiden and Miss Beryl Splatt for biochemical data, and to Miss Hania Ayzner for technical assistance.

REFERENCES

Allison, A. C., and ap Rees, W. (1957). *Brit. med. J.*, **2**, 1137.
Chaplin, H., jun., and Mollison, P. L. (1953). *Clin. Sci.*, **12**, 351.
Gornall, A. G., Bardawill, C. J., and David, M. M. (1949). *J. biol. Chem.*, **177**, 751.
Hawk, P. B., Bergeim, O., Oser, B. L., and Cole, A. G. (1937). *Practical Physiological Chemistry*, 11th ed. Blakiston, Philadelphia.
Jayle, M. F., and Boussier, G. (1955). *Expos. ann. Biochim. méd.*, **17**, 157. Quoted by Laurell and Nyman (1957).
Laurell, C-B., and Nyman, M. (1957). *Blood*, **12**, 493.
Mackay, I. R., Taft, L. I., and Cowling, D. C. (1956). *Lancet*, **2**, 1323.
Malloy, H. T., and Evelyn, K. A. (1937). *J. biol. Chem.*, **119**, 481.
Nosslin, B. F., and Nyman, M. (1958). *Lancet*, **1**, 1000.
Nyman, M. (1957). *Scand. J. clin. Lab. Invest.*, **9**, 168.
—— (1958a). *Clin. chim. Acta*, **3**, 111.
—— (1958b). Unpublished data, quoted by Nosslin and Nyman (1958).
Owen, J. A., Silberman, H. J., and Got, C. (1958). *Nature (Lond.)*, **182**, 1373.
Polonovski, M. (1945). *Schweiz. med. Wschr.*, **75**, 859.
—— and Jayle, M. F. (1940). *C.R. Acad. Sci. (Paris)*, **211**, 517.
Raffensperger, E. C. (1958). *Ann. intern. Med.*, **48**, 1243.
Reitman, S., and Frankel, S. (1957). *Amer. J. clin. Path.*, **28**, 56.
Smithies, O. (1955). *Biochem. J.*, **61**, 629.
Watson, C. J. (1939). *Ann. intern. Med.*, **12**, 1782.
Wood, I. J. (1959). Submitted for publication.

Medical Memoranda

Retention of Islets of Sensation in Cervical Cord Injury

The following two cases are reported because of their interest and because I have failed to find a note of similar cases.

CASE 1

At midday on December 6, 1947, a farmer aged 52 was out hunting. While walking his horse on the hard road from one draw to another it suddenly pecked and he was thrown to the ground. He immediately became helpless and was admitted to hospital. He arrived at 1.5 p.m. and I saw him soon afterwards. He was conscious, co-operative, and sensible, and his only complaint was that he had lost the use of his limbs. It was difficult to know exactly what had happened, but from the appearance of his hard hat it was assumed that he had landed on the back of his head.

On examination there was no sensation in his body or in the arms or legs, and there was a total quadriplegia. The reflexes in the legs were brisk and an ankle clonus was present. The plantar responses were extensor, and it was noticed that touch sensation was still present in the soles of both feet. An *x*-ray examination did not help in determining the anatomical lesion. At 3.30 p.m. the area of loss of sensation had diminished and was now from below the first ribs and below the insertion of the deltoid muscles. Sling traction was applied, but this caused so much discomfort that after some hours it was replaced by skeletal traction by calliper, and this made the patient much more comfortable. His condition, however, gradually deteriorated and he died at 7 p.m. on December 8.

A post-mortem examination was made by Dr. Ian Mackenzie. It was found that, although there was no fracture, the body of the fourth cervical vertebra could be moved on the body of the fifth because there was some tearing of the anterior longitudinal ligament. In the cervical region there was some extradural haemorrhage and the cord appeared to be congested. Section of the cord showed some blood in the central canal. There was nothing otherwise significant in the examination.

CASE 2

At 8 p.m. on April 3, 1955, a miner aged 55 stepped on the colliery belt, which gave way and he fell on the pans. He immediately became helpless and was admitted to hospital. He arrived at 10.30 p.m. and I saw him soon after.

On examination there was a quadriplegia and an area of anaesthesia below a line from the left axilla to the right anterior spine of the pelvis. There was also anaesthesia on the inner surfaces of both arms and the whole of the forearms. The reflexes were exaggerated and the plantar responses were extensor. When ascertaining the nature of the plantar responses it was noted that epicritic and protopathic sensation was still present in the soles of both feet. An *x*-ray examination did not help in deciding on the anatomical lesion. Sling traction was applied and for a day or two the patient, who was quite co-operative, appeared to be holding his own, but on April 7 signs developed at both bases and he deteriorated, dying on April 9.

A post-mortem examination was made by Dr. E. W. N. Trounson, the material findings being as follows: The anterior longitudinal ligament was ruptured between the sixth and seventh cervical vertebrae and there was a horizontal tear in the lower part of the intervertebral disk. The vertebral bodies above were hyperextended. External examination of the cord showed barely detectable contusions in the lower cervical region. The lungs were congested and grossly oedematous, with widespread ill-defined pneumonic consolidation at both bases. There was also fairly well marked dust pigmentation with focal emphysema. Dr. Trounson attributed death to hypostatic pneumonia and contusion of the spinal cord. The cord was subsequently examined microscopically, and this showed some tiny haemorrhages within its substance.

COMMENT

When I first saw Case 1 my impression was that the patient had probably sustained a contusion of the cord from which he was possibly going to recover, but I had never before found such a large anaesthetic area containing islands of sensation in the soles of the feet. As I knew that Mr. Leslie Morris, of Leicester, had a large experience of cord injuries in miners, I discussed the case with him over the telephone and he was so interested that he came to see the patient and confirmed my findings. When the second patient developed signs in the chest I asked Dr. Wakes Miller to see him, and he also was most interested in the fact that these islands of sensation had persisted.

Both patients were men of approximately the same age with similar lesions. Both had sustained hyperextension injuries in the cervical region with tears of the anterior longitudinal ligament and consequent damage to the cervical cord. In both patients the fibres conveying sensation from the soles of the feet had escaped damage. These, I understand, run on the surface of the cord posteriorly in this region. It is not difficult, therefore, to understand that they would be the last to sustain damage by hyperextension.

These two cases may have exhibited a rare phenomenon, but I cannot help feeling that retention of sensation in the soles of the feet may persist in cervical cord injuries much more often and is overlooked when the loss-of-sensation area is mapped out. It was not until I had noted it in the first case that I looked for it in others.

D. S. PRACY, F.R.C.S.Ed.,
Formerly Surgeon, Nuneaton and Coventry and Warwickshire Hospitals.

Reviews

TENTH EDITION OF "JOSLIN"

The Treatment of Diabetes Mellitus. By Elliott P. Joslin, Howard F. Root, Priscilla White, and Alexander Marble. Tenth edition. (Pp. 798; illustrated. £6 2s. 6d.) London: Henry Kimpton. 1959.

The first edition of this book was published in 1916, five years before the discovery of insulin; since then it has become the standard textbook on the subject and better known by the name of its author than by its title.

The general form of the tenth edition of "Joslin" follows that of previous ones, but with special emphasis on prevention or deferment of onset and on control of diabetes. The views expressed are largely based on the personal experience of the authors and the statistical evaluation of their very extensive clinical material; this adds to the value of the book, but inevitably results in some degree of dogmatism on controversial issues. For example, a good case is made out for the Mendelian recessive theory of inheritance which might well lead the reader to believe that this view is now generally accepted. In other connexions, however, such as the causal relationship between trauma and diabetes, a dogmatic attitude provides help where it is most needed. Under the heading of "the physiology of diabetes" A. E. Renold gives a short but up-to-date account of modern views on intermediary carbohydrate metabolism and the action of insulin and oral hypoglycaemic agents, and there is an excellent chapter by Shields Warren and P. M. Le Compte on the pathology of the disease. The attitude adopted towards the sulphonylureas is wise, and that towards phenethylbiguanide (D.B.I.) as cautious as the drug's similarity to "synthalin" demands. The use of hormones in diabetic pregnancy is still advocated, but Joslin raises a doubt in his first chapter as to whether Dr. Priscilla White's low foetal mortality rate may not be due in large measure to her good management and control of the maternal diabetes.

This book is essentially one for reference rather than consecutive reading, but for those concerned with the treatment of diabetes or the giving of expert evidence on this subject the possession of "Joslin" is essential. And it is indeed remarkable that the senior author has been able to pilot through the press this latest edition on the eve of his ninetieth birthday.

WILFRID OAKLEY.

TROPICAL PAEDIATRICS

Diseases of Children in the Subtropics and Tropics. By H. C. Trowell, O.B.E., M.D., F.R.C.P., and D. B. Jelliffe, M.D., M.R.C.P., D.C.H., D.T.M.&H. (Pp. 919+xvi; illustrated. £5 5s.) London: Edward Arnold (Publishers), Ltd. 1958.

The case for paediatrics as a separate specialty having been made, it is logical that specialist paediatric services should evolve in the Tropics, and this book is to be welcomed as an aid to this. It is clear also that in tropical regions, many of which are underdeveloped, numerous paediatric problems exist which do not occur in regions which are either cooler or more advanced. Broadly speaking, they consist of those caused by parasitic and other zymotic diseases met with exclusively or almost exclusively in warm climates, and, secondly, the special nutritional, social, and other paediatric conditions resulting from underdevelopment of a territory, bad hygiene, and climate. The parasitic and other zymotic diseases in the Tropics differ comparatively little from those caused in adults by the same organisms. The editors of this volume are therefore to be complimented for having drawn heavily upon non-paediatric specialists in these diseases for what constitutes the greater part of the book.

Those who go to the Tropics see there many conditions which are also found in cooler climates; some are misled by this into believing that special tropical diseases are rare and that medicine in the Tropics is similar to that in temperate regions. This attitude usually springs from lack of training in tropical medicine, the result is an unawareness, and so lack of recognition of the manifestations of tropical diseases. The editors have, however, clearly realized the importance of special tropical diseases, as is evidenced by the space given to conditions caused by parasitic and zymotic agents. The special problems relating to infant and child welfare in backward countries are thoroughly dealt with, as is to be expected, for the editors have placed these subjects among their special interests. The claim is made that only the commoner diseases are discussed, and, though not all paediatricians in a lifetime will encounter all the diseases here considered, the commoner ailments are certainly given prominence.

In a volume containing contributions from over 70 persons it is not to be expected that the style will be uniform, but the variations do not jar the reader. There is no other comprehensive volume exclusively devoted to this subject, and this one therefore fills a gap; it will be a valuable addition to the library of those practising in the hot countries.

A. W. WOODRUFF.

THUDICHUM

Thudichum. Chemist of the Brain. By David L. Drabkin. (Pp. 309; illustrated. 40s.) Philadelphia: University of Pennsylvania Press. London: Oxford University Press. 1958.

Professor Drabkin in his biography of Thudichum has created a vivid picture of a Victorian scientist, the way he lived and worked, and of his relationship with his contemporaries. Thudichum was born in 1829 and died in 1901, and spent the whole of his life working on the nature of the lipoidal substances present in the central nervous system. The work is a little involved in style and has to be read very carefully. The author is so interested in his subject that he tends to dart about chronologically, and this can be quite confusing. He delights in statements like the following:

> "Thudichum died in 1901; I first met him in 1924. I was a postmedical fellow in Professor Lafayette B. Mendel's laboratory at Yale. My research was on urochrome, the normal pigment of the urine. Thudichum had gotten there first; sixty years earlier he had christened the pigment."

The first part of the book deals with Thudichum as a man; the second part with his time and contemporaries; and the third, and perhaps the most interesting from the biochemical point of view, with his actual publications and works. It is highly possible that the book will be read by different people for different reasons. Those interested in the historical aspect will be interested in the first two parts, while the more technically minded will turn to the third part. It is this division that gives the impression of discontinuity, but

if read as a whole the work provides a remarkable picture of chemical science as applied to biological material in the latter half of the nineteenth century.

The book is obviously a labour of love and must represent a truly incredible amount of close application to detail. It is dedicated to Otto Rosenheim, a distinguished British investigator in the same field and himself a great supporter of Thudichum. In conclusion, a very valuable contribution to scientific biographies.

E. C. DODDS.

WORLD HEALTH

World Health. By Fraser Brockington. (Pp. 405; illustrated. 5s.) London: Penguin Books. 1958.

This book is topical, as it was written during the year when the World Health Organization was celebrating its tenth anniversary. It contains a foreword by Dr. A. E. Clark-Kennedy, the General Editor of the Pelican Medical Series, and another by Dr. M. G. Candau, Director-General of W.H.O. The modest price puts it within the reach of all.

The importance is stressed of paying regard, when health projects are being introduced into undeveloped countries by Western experts, to traditional customs, beliefs, and even superstitions. There is much in the book on the relationship between industrial occupations and health. The spread of industrialization to peasant countries is regarded as inevitable, and the experience of countries earlier in the field should be used so that the "enduring mischief to health" of the Industrial Revolution which started in England may be avoided. The demands of increased population, the result of a stable and high birth rate and a falling death rate, on food supplies and housing are well brought out. In undeveloped countries there are now the same defects in the environmental sanitary services as were present in England when Sir Edwin Chadwick started his great campaign to introduce "The Sanitary Idea." Professor Brockington rightly says, "Public Health is rooted in the environment, in the way people live, in the social factors of the home and the workshop."

No single pattern for the application of preventive measures is universally right, and there are excellent summaries of the administrative structure in many countries, including the U.S.A., India, Ceylon, Japan, Yugoslavia (which is given high praise), Turkey, Russia, and Thailand. The evolution of international public health and the work of W.H.O. are dealt with adequately. It is stated that already "operations against malaria, tuberculosis, and treponemal infections have benefited 400 million people," and that the World Health Organization is a valuable new tool at the disposal of Governments.

The last 100 pages are devoted to "The Measurement of Health" and the endeavours being made to acquire accurate information. This part contains enough material for a separate book, and discusses in considerable detail the standard classification of disease, sampling methods, and surveys to ascertain the incidence of ill-health—essential information for research, planning, and evaluation of results.

The book achieves the purpose for which it is intended and can be highly recommended. The only possible criticism—and it is quite minor—is that something smaller would be more likely to be read from cover to cover.

ALLEN DALEY.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Inborn Errors of Metabolism. By David Yi-Yung Hsia, M.D. (Pp. 358; illustrated. 72s.) Chicago: The Year Book Publishers. London: Interscience Publishers Ltd. 1959.

Surgery of the Prostate. By Henry M. Weyrauch, M.D., F.A.C.S. (Pp. 535+xii; illustrated. £5 5s.) Philadelphia, London: W. B. Saunders Company. 1959.

Fundamentals of General Anesthesia for Students and Practitioners of Dentistry. By John Adriani, M.D. (Pp. 213+xvii; illustrated. 50s.) Oxford: Blackwell Scientific Publications. 1959.

Vascular Spiders and Related Lesions of the Skin. By William Bennett Bean, M.D. (Pp. 372+xix; illustrated. 63s.) Oxford: Blackwell Scientific Publications. 1958.

Perspectives in Virology. A Symposium. Edited by Morris Pollard. (Pp. 312+xix; illustrated. 56s.) New York: John Wiley and Sons, Inc. London: Chapman and Hall, Ltd. 1959.

Adoption. By Margaret Kornitzer. (Pp. 176. 10s. 6d.) London: Putnam. 1959.

Miscellaneous Notes (Second Series). By F. Parkes Weber, M.D., F.R.C.P., F.S.A. (Pp. 20. 5s.) London: H. K. Lewis and Co. Ltd. 1959.

A Text on Systemic Pathology. Volume II. Edited by Otto Saphir, M.D. (Pp. 1,950+xvi; illustrated $38.) New York, London: Grune and Stratton. 1959.

A Short History of Psychiatry. By Edwin H. Ackerknecht. Translated from the German by Sulammith Wolff, M.A., M.R.C.P., D.P.M. (Pp. 98+vi; illustrated. 25s.) New York, London: Hafner Publishing Company. 1959.

Fracture Surgery. A Textbook of Common Fractures. By Henry Milch, M.D., and Robert Austin Milch, M.D. With a chapter on Anaesthesia by Herbert D. Dubovsky, M.D. (Pp. 470+x; illustrated. £7.) New York: Paul B. Hoeber, Inc. London: Pitman Medical Publishing Co. Ltd. 1959.

Hernia. By Sir Heneage Ogilvie, K.B.E., M.A., M.Ch., M.D., F.R.C.S. (Pp. 135; illustrated. 28s.) London: Edward Arnold (Publishers) Ltd. 1959.

Radiation Biology and Cancer. A Collection of Papers Presented at the Twelfth Annual Symposium on Fundamental Cancer Research, 1958. (Pp. 493; illustrated. $8.50.) Austin, Texas: University of Texas Press. 1959.

Manual of Differential Diagnosis. By William C. Matousek, M.D. (Pp. 352. 60s.) Chicago: The Year Book Publishers. London: Interscience Publishers, Ltd. 1959.

Practical Leads to Puzzling Diagnoses. Neuroses that run through Families. By Walter C. Alvarez, M.D., D.Sc. (Pp. 490+x. 72s.) Philadelphia, Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1959.

Applied Anatomy for Nurses. By E. J. Bocock, S.R.N., S.C.M., D.N., and R. Wheeler Haines, M.B., D.Sc., F.L.S. Second edition. (Pp. 326+xii; illustrated. 17s. 6d.) Edinburgh, London: E. and S. Livingstone, Ltd. 1959.

A System of Orthopaedics and Fractures. By A. Graham Apley, M.B., B.S., F.R.C.S. (Pp. 357+vii. 47s. 6d.) London: Butterworth and Co. (Publishers) Ltd. 1959.

Principles and Practice in the Management of Surgical Patients. By A. Venugopal Mudaliar, M.S., F.A.C.S., F.I.C.S. (Pp. 500+xii; illustrated. 30s.) Madras: G. S. Press. 1959.

History of American Medicine. A Symposium. Edited by Felix Marti-Ibañez, M.D. (Pp. 181. $4.) New York: MD Publications, Inc. 1959.

Viral and Rickettsial Infections of Man. Edited by Thomas M. Rivers, M.D., and Frank L. Horsfall, Jr., M.D. Third edition. (Pp. 967+xviii; illustrated. £3 3s.) London: Pitman Medical Publishing Co. Ltd. 1959.

The Year Book of Drug Therapy, 1958-1959. Edited by Harry Beckman, M.D. (Pp. 569; illustrated. 57s.) Chicago: The Year Book Publishers. London: Interscience Publishers. 1959.

The Year Book of Ophthalmology, 1958-1959. Edited by Derrick Vail, B.A., M.D., D.Ph.(Oxon.) F.A.C.S., F.R.C.S. (Hon.). (Pp. 407; illustrated. 57s.) Chicago: Year Book Publishers. London: Interscience Publishers, Ltd. 1959.

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FOR AND AGAINST B.C.G.

There can be few immunization procedures which have roused more interest and argument than B.C.G. vaccination. Its advocates and its antagonists are still eager to air their views, and there seems little likelihood of either side's converting the other. Where lies the truth? If B.C.G. is of proved value in increasing resistance to tuberculosis, and is safe, it is our duty to recommend its use for all our patients liable to be exposed to the infection. And who can say when such exposure may occur? We do not hesitate to advise vaccination against smallpox, though the likelihood of exposure to that infection is remote in Great Britain—certainly far more remote than is the risk of encountering tuberculosis. But smallpox vaccination is undertaken primarily as a general public health measure to ensure that an adequate proportion of the population would be protected if an epidemic arose. Protection against tuberculosis is usually regarded as a personal protection—for the individual rather than for the community—though in countries where tuberculosis is widespread it may assume a twofold importance: individual protection and prevention of the spread of infection.

Is it of proved value? This is the question about which arguments grow most heated. Unfortunately for its advocates there is no test comparable to those applicable to diphtheria and tetanus toxoids or to pertussis and poliomyelitis vaccines. All that is proved beyond doubt is that satisfactory B.C.G. vaccination results in tuberculin allergy. The relationship between allergy and immunity remains complicated and is still obscure. If vaccinated people in a community have a lower incidence of tuberculosis than non-vaccinated, this is not, say the antagonists, proof that they escaped infection because of their vaccination. Nor can its advocates provide this proof, though they accept the implication that the B.C.G. had protected against infection. On one thing both parties agree—that general measures of hygiene and scrupulous care in case finding, segregation, and therapy are of prime importance in the final eradication of tuberculosis in any country.

In an article at p. 1423 of the *Journal* this week a number of American physicians, Dr. A. S. Anderson and his colleagues, support and explain the "anti-B.C.G." attitude, and some recent American studies were discussed in these columns last year.[1] The present paper may not convince the advocates of B.C.G. vaccination, though the weakness of the evidence for it is revealed in the article by Drs. J. Lorber and Peggy C. Menneer (p. 1430), in which the authors say: "As there were no comparable controls it cannot be shown conclusively that B.C.G. vaccination prevented tuberculosis in this group of infants. Nevertheless the results are highly suggestive that this, in fact was the case." It is the "highly suggestive" results which have been consistently obtained by the advocates which have encouraged them to pursue their work, and while they are able to continue producing such results they will certainly continue to use and recommend B.C.G. It is the lack of conclusive proof which provides the antagonists with their ammunition.

The question of the safety of B.C.G. is as important as the results of using it. The crux of the matter is whether the vaccine is a *virus fixe* as Calmette averred so long ago as 1927. Now Anderson and his colleagues cast doubts on this and consider that it has yet to be proved. Nevertheless, so many millions of people have been given B.C.G., and there have been so few fatalities (less than half a dozen recorded), that it is clear that the risk of progressive tuberculosis in consequence of vaccination is vastly less than, for example, the risk of acquiring poliomyelitis after poliomyelitis vaccine.

It is true that some ill-effects from B.C.G. vaccination have been reported—as, for example, the case recorded by Drs. Philip Ellman and L. G. Andrews at p. 1433—but the morbidity varies with the antigenicity of the vaccine and the number of viable organisms injected, and can virtually be produced, or reduced to zero, at will when the vaccinator knows what vaccine he is using. S. R. Rosenthal, one of the chief advocates of B.C.G. in the U.S.A. (whose writings, incidentally, receive no mention in the article by Anderson and his colleagues), points out that changes in the strain of B.C.G. undoubtedly occur, depending on the method of cultivation, but generally are not permanent and tend towards increased attenuation rather than enhanced virulence. He has stated[2]: "Of the numerous reports cited where B.C.G. vaccination was part of an over-all tuberculosis control programme and where the vaccinated and non-vaccinated groups were comparable, it can be stated unequivocally that B.C.G.

[1] *Brit. med. J.*, 1958, 2, 374.
[2] Rosenthal, S. R., *BCG Vaccination against Tuberculosis*, 1957, Boston.
[3] First (Progress) Report to the Medical Research Council by their Tuberculosis Vaccines Clinical Trials Committee, *Brit. med. J.*, 1956, 1, 413.

affords a decided protection against virulent superinfection." The Medical Research Council's trial in Great Britain[3] gives convincing support to this statement.

As the net is closing round tuberculosis, it is worth considering whether, even if B.C.G. vaccination is of value, it is any longer necessary. Three particular points arise here. The first is that nowadays exposure to infection is more likely to come from an unsuspected than a known source, and is therefore more difficult to prevent. The second is that infants resist tuberculosis poorly. And the third is that once a person has been infected it is impossible to be sure that endogenous reactivation may not occur even after many years of apparent "cure," and despite the excellent results obtained with isoniazid in therapy. Protection, if it is to be of greatest value, should therefore be offered as soon as possible after birth. It is likely that a simple, effective, multiple-puncture technique may soon be available, and routine vaccination in infancy would then become as practicable as vaccination against smallpox. Many believe this would be a valuable addition to the immunization schedule for infants in Great Britain, for, despite the contrary view, and admitting the difficulties of confirming by scientifically controlled trials the efficacy of B.C.G. vaccination, they consider that the results of vaccination have proved so outstanding that its administration should be continued and even extended. Certainly any doctor, when asked by parents if their children should receive B.C.G., must consider very carefully the implications of denying them this measure. If vaccination is not undertaken in infancy, it should be done before the onset of puberty, and should therefore be offered between 10 and 12 years. This is better than leaving it until school-leaving age, as is the present practice, for puberty adds to the hazards of tuberculosis.

PROGNOSIS OF HYPERTENSION

What is the prognosis in hypertension? Which hypertensive patients require treatment? What treatment should they have? These were among the questions discussed in two articles in last week's *Journal*, the first by Dr. A. W. D. Leishman[1] and the second by Drs. M. J. D. Newman and J. I. S. Robertson.[2] Widespread evidence exists that modern medical treatment greatly improves the prognosis of those patients with hypertension whose expectation of life would otherwise be poor. But perseverance with effective treatment imposes some burden on the patient: side-effects may further incommode him, and a slight risk is attached to some forms of therapy. While these are discomforts the hypertensive patient who needs treatment can well tolerate, it is obviously undesirable to impose them unnecessarily.

Repeated examination of the blood pressure under basal conditions may show that slight hypertension, found under the excitement and apprehension of an initial medical examination, readily disappears. On the other hand, persistence of the diastolic pressure at levels of 95–110 mm. Hg or more merits further investigation, especially in younger patients. The full examination of these patients may require facilities which are not usually available to the family doctor. It has to be decided whether the hypertension is essential or secondary to some cause such as renal disease, coarctation of the aorta, phaeochromocytoma, Cushing's disease, renal arterial occlusion, or aldosteronism. If essential hypertension is the correct diagnosis, then a search for the complications of hypertension is important because of their bearing on prognosis and the need for treatment. The prognosis in essential hypertension is related more to the effect of hypertension on vital functions than to height of the blood pressure itself. Thus the condition of the heart, kidneys, ocular fundi, and brain is particularly important. If function is significantly impaired appropriate measures to lower the blood pressure are needed. G. A. Perera[3] found in 500 patients with raised blood pressure that the average age at onset of their disease was 32 years and at death 52. The commonest cause of death is from cardiac complications, especially heart failure. Once papilloedema has developed the outlook without treatment is very poor. J. McMichael[4] found that most hypertensive patients with papilloedema had progressive renal deterioration and were dead within a year.

What of the patient with a significantly high diastolic pressure who has no evidence of functional impairment when seen? Some advise treatment for these cases as a preventive measure, others have stressed that the condition may remain unchanged for years and hesitate to initiate a regime of active treatment. Certainly if these patients are not treated with hypotensive drugs they must be carefully watched for complications. A rise in the systolic pressure with a normal diastolic pressure is commonly seen with advancing years and the

[1] Leishman, A. W. D., *Brit. med. J.*, 1959, **1**, 1361.
[2] Newman, M. J. D., and Robertson, J. I. S., ibid., 1959, **1**, 1368.
[3] Perera, G. A., *J. chron. Dis.*, 1955, **1**, 33.
[4] McMichael, J., *Brit. med. J.*, 1952, **1**, 933.
[5] Abrahams, D. G., and Wilson, C., *Lancet*, 1957, **1**, 68.
[6] McDonald, L., and Goldberg, B., ibid., 1957, **1**, 77.
[7] Uchigasaki, S., *Tôhoku J. exp. Med.*, 1955, **61**, 245.
[8] Szent-Györgyi, N., *Circulation*, 1956, **14**, 17.
[9] Platt, R., *Quart. J. Med.*, 1947, **16**, 111.
[10] Søbye, P., *Heredity in Essential Hypertension and Nephrosclerosis*, 1948. Copenhagen.
[11] Pickering, G. W., *Ann. intern. Med.*, 1955, **43**, 457.
[12] Brod, J., and Fencl, V., *Cas. Lék. ces.*, 1958, **97**, 1025.

development of arterial degeneration. This systolic hypertension does not indicate a poor prognosis, nor does it usually require treatment.

An array of powerful drugs to lower blood pressure is now available, but the value of simple measures should not be overlooked, or the fact that none of these drugs is ideal. Modification of the patient's way of life, weight reduction in the obese, sedation, and sodium depletion by either diet or drugs, all have an important part to play in the management of the hypertensive patient. Most will reserve such surgical procedures as sympathectomy and adrenalectomy for patients in whom medical treatment has failed. Mecamylamine, one of the most effective hypotensive drugs, acts by blocking the autonomic ganglia. Ganglion-blocking drugs have proved easier to use than hypotensive drugs with a reflex action, such as protoveratrine. Those which act on the brain stem, such as rauwolfia derivatives, are useful adjuncts to ganglionic blockade. Hydrallazine, which acts both centrally and peripherally, may have a particular place in the treatment of patients with severely damaged kidneys, for it selectively maintains the renal blood flow. Impaired renal function may sometimes worsen critically during hypotensive therapy.[5 6]

The incidence of hypertension is probably increasing as more people reach the age when it is most common. The aetiology of essential hypertension remains obscure. It is not even known why women withstand hypertension much better than men. An environmental factor in hypertension is likely,[7 8] and a familial factor obvious. The latter is useful in separating essential from other forms of hypertension. Hypertension may be a hereditary disease[9-11] conveyed as a Mendelian dominant, but the inherited factor may represent only a tendency to arterial or arteriolar change in renal, coronary, or cerebral vessels, and may not be a specific factor for hypertension. Any reluctance to regard essential hypertension as a specific disease should not preclude awareness of its unfortunate complications. In uncomplicated hypertension the cardiac output is well maintained. It follows, therefore, that the total peripheral vascular resistance must be increased. A better understanding of this disordered mechanism itself should lead to a more accurate estimation of the prognosis in any individual patient and to the more efficient control of his hypertension. J. Brod and V. Fencl's[12] studies led them to the view that in hypertension the vascular bed relaxes inadequately during the diurnal surges of cardiac output, or even that it may actively contract. Their work will be followed with the greatest interest by all who have to treat hypertensive patients.

PEPTIC ULCER IN AFRICANS

While the clinical frequency of the disorder is difficult to estimate because of conditions of medical practice, many reports from doctors who have worked for long periods in Africa confirm that peptic ulcer is seldom encountered. Thus, of 7,019 operations performed in a Uganda hospital twenty years ago, only 30 were for ulcer,[1] while in Lagos M. Ellis[2] had performed, up to 1948, only 191 operations for ulcer in six years of busy surgical practice. In both series perforations were surprisingly rare. While in a few parts of the continent some observers have noted the occurrence of ulcers in Africans[3-8] the overall impression gained by L. S. P. Davidson[9] in 1954, after discussions with physicians throughout Africa, was of the extreme rarity of the disease. But because a satisfactory history is often unobtainable and radiological facilities are unavailable it might be more accurate to state that ulcer often fails to come to the notice of the practising physician or surgeon in Africa.

Pathological reports also give the impression that ulcers are rare; they caused only 3 deaths in a series of 947 necropsies reviewed[1] in Uganda in 1937 and only 8 deaths in 8,328 necropsies at the Government mortuary in Johannesburg between 1928 and 1937.[10] As an incidental finding ulcers seemed equally uncommon, being discovered on 3 occasions in 1,020 necropsies performed in Uganda between 1947 and 1949,[11] and on 5 occasions in 1,144 necropsies performed at a Johannesburg hospital between 1927 and 1935.[10] However, there are many pitfalls in the assessment of the incidence of peptic ulcer from necropsy reports,[12 13] especially when, as in these series, most of the analyses were done retrospectively and when there was no fixed intention by the pathologists to record all ulcers and scars at the time the examination was made. Like clinical reports, therefore, the necropsy records probably express only the proportion of cases in which ulcer appeared as an obtrusive event.

In an attempt to estimate the overall frequency of peptic ulcer and to discover any variations in its incidence among different tribes in Uganda, A. Raper[14] carried out a planned prospective survey in Kampala. Between 1951 and 1956 he and his co-workers carried out 776 post-mortem examinations, either in hospital or in police mortuaries, and particular care was taken to record all ulcers and scars present. The subjects—647 males and 129 females—came from various tribes. A surprisingly high incidence of ulcers was found, reaching 15.3% in men and 4.7% in women. The frequency of

[1] Roberts, C. E., *E. Afr. med. J.*, 1937, **14**, 88.
[2] Ellis, M., *Brit. J. Surg.*, 1948, **36**, 60.
[3] Vassallo, S. M., *E. Afr. med. J.*, 1937, **14**, 83.
[4] Goodchild, R. T. S., ibid., 1949, **26**, 138.
[5] Sergel, C. J. S., ibid., 1952, **29**, 271.
[6] Buxton, K. L., *Lancet*, 1954, **2**, 1231.
[7] Ceuterick, J., *Ann. Soc. belge Méd. trop.*, 1955, **35**, 119.
[8] De Becker, R., ibid., 1957, **37**, 127.
[9] Davidson, L. S. P., *Lancet*, 1954, **1**, 614.
[10] Eagle, P. C., and Gillman, J., *S. Afr. J. med. Sci.*, 1938, **3**, 1.
[11] Raper, A. B., *E. Afr. med. J.*, 1949, **26**, 137.
[12] Ivy, A. C., Grossman, M. I., and Bachrach, W. H., *Peptic Ulcer*, 1950, Philadelphia.
[13] Watkinson, G., *Schweiz. Z. Path.*, 1958, **21**, 405.
[14] Raper, A. B., *Trans. roy. Soc. trop. Med. Hyg.*, 1958, **52**, 535.

duodenal ulcer was six times that of gastric ulcer. In men, ulcers became progressively more common in successive decades—increasing from 6.3% in the second to 15.3% in the fourth, and reaching 27% in the sixth. These figures do not differ materially from ulcer frequencies in men of similar age as assessed by G. Watkinson[13] in a recent post-mortem survey in England and Scotland. While Raper found intertribal differences in the occurrence of ulcers, the series was too small to establish these statistically.

There are several possible reasons why this pathological estimate of the incidence of peptic ulcer in Africans so far exceeds clinical experience. The doctor may be hampered by language difficulties which interfere with the taking of a full history and may tend too often to ascribe abdominal symptoms to "worms" or to "constipation," while the African's appreciation and interpretation of his pain may be very different from that of a European. Regional differences in the incidence of ulcer probably exist because of variations in tribal eating and drinking habits. The improving life expectancy, nutrition, and educational status of the African may perhaps have been accompanied by an increased tendency to develop ulcers. Raper's survey shows that peptic ulcer in fact occurs commonly in the African but is at present likely to pass unrecognized clinically—a defect which improved diagnostic facilities might help to remedy.

HAPTOGLOBINS IN HEPATIC DISEASE

In recent years some of the serum proteins have been shown to have the remarkable property of specifically binding certain biologically important metals or compounds. Deficiency of any of these proteins may be associated with specific diseases. The best studied is the copper-binding protein coeruloplasmin.[1] Deficiency of it is characteristically found in hepatolenticular degeneration (Kinnier Wilson's disease).[2] Much is also known of the protein that specifically binds iron,[3] and, more recently, of the group of proteins termed haptoglobins, which are characterized by their ability to bind haemoglobin.[4]

Though the haptoglobins were first described about 25 years ago, O. Smithies[5] reawakened interest in them. He showed by starch electrophoresis that there are at least three different proteins of this kind in human serum and that their presence is hereditarily determined. A. C. Allison and W. A. Rees[6] showed that they play an important part in preventing the loss of haemoglobin via the kidneys.

Now Drs. J. A. Owen, I. R. Mackay, and Miss Catherine Got show in a paper at p. 1454 of the *Journal* this week that the level of the serum haptoglobins may be influenced by disease of the liver. The concentration of the haptoglobin in the serum was estimated by adding a haemoglobin solution to the serum until the haptoglobin was saturated; the end point was determined by finding free haemoglobin when the mixture was subjected to electrophoresis on paper. The mean level of haptoglobins in 50 normal subjects was 84 mg. per 100 ml. of serum. Patients with parenchymal disease—for example, acute or chronic hepatitis—showed a mean level of about half this, whereas in 12 patients with extrahepatic biliary obstruction the mean level was 185 mg. per 100 ml. It appears, therefore, that the level of haptoglobin in the serum might be of diagnostic value in distinguishing parenchymal from obstructive jaundice, and the figures given by Owen and his colleagues strongly support this idea. Thus in 14 cases of hepatitis the mean level of haptoglobin was 35 mg. per 100 ml. of serum and exceeded 90 mg. per 100 ml. in only 1 case, whereas in 12 cases of obstructive jaundice the mean level of haptoglobin was 185 mg. per 100 ml. and exceeded 90 mg. in all but one.

From these and other results which these authors present it appears that the level of serum haptoglobin, like the level of serum albumin, can be correlated with the results of other tests of hepatic function. Much evidence suggests that the serum albumin is secreted by the liver. Are we therefore to conclude that the haptoglobins also are produced by the liver cells?

[1] Holmberg, C. G., and Laurell, C. B., *Acta chem. scand.*, 1947, **1**, 944.
[2] Scheinberg, H., and Gitlin, D., *Science*, 1952, **116**, 484.
[3] Schade, A. L., and Caroline, L., ibid., 1946, **104**, 340.
[4] Polonovsky, M., and Jayle, M. F., *C.R. Acad. Sci. (Paris)*, 1940, **211**, 117.
[5] Smithies, O., *Biochem. J.*, 1955, **61**, 629.
[6] Allison, A. C., and Rees, W. A., *Brit. med. J.*, 1957, **2**, 1137.

PLASTIC BAGS

Transparent plastic bags are increasingly used for wrapping goods of different kinds—vegetables, clothes, and toys, for example. Some of them are quite big. They are convenient and hygienic, but in some circumstances they are death-traps.

Last September[1] there was an inquest at Welwyn Garden City into the death of a 4-year-old boy who had put a "polythene" bag over his head. He died of asphyxia. In recording a verdict of misadventure the Welwyn coroner drew attention to this hazard. "I understand the police have found other children playing with polythene bags," he said, "and obviously there is a danger of this kind of thing happening again." A near fatality with a "cellophane" bag is reported in our correspondence columns this week by a doctor in Northumberland (p. 1478). A more alarming report[2] comes from the U.S.A., however. In Phoenix, Arizona, it came to the notice of Dr. P. B. Jarrett, chairman of the county medical society's safety committee, that four children there had recently suffocated while playing with plastic "garment bags." Making further inquiry, he found that increasingly laundries and dry-cleaning establishments in the Phoenix area—as elsewhere in the United States—were using these bags. A general alarm was therefore sounded through the American Medical

[1] *The Times*, September 30, 1958.
[2] *J. Amer. med. Ass.*, 1959, **169**, 2021.
[3] *The Times*, May 27, 1959.
[4] Ibid., May 19, 1959.
[5] *Brit. med. J.*, 1958, **2**, 111.
[6] *The Registrar-General's Statistical Review of England and Wales for the Year 1957*. Part I, 1959, H.M.S.O., London.

Association and the press, and further fatal cases soon came to light. The U.S. National Safety Council has reported 28 cases so far this year.[3] It seems that the bags become electrically charged, and, if placed over a child's head, they cling tenaciously and resist removal. What appears to be a tempting toy can thus become an instrument of quick suffocation.

In North America this hazard has been taken very seriously. A Bill has already been introduced in Congress to compel manufacturers to print warning notices on every bag.[4] In Canada, after the death of a 10-month-old child at Windsor last month, the chief coroner of Ontario has called for their banning.[3] It is too early perhaps to judge the gravity of the risk over here, though the Welwyn case and the case reported by our Northumberland correspondent show that it exists. A year ago a paediatric correspondent, discussing in our medico-legal column suffocation in infancy,[5] warned against too ready acceptance of mechanical suffocation as an explanation of unexpected "cot deaths." In 1957 162 infants under 1 year of age were registered as dying in England and Wales from accidental mechanical suffocation.[6] After reviewing the evidence, he concluded that such a diagnosis demanded, first, the presence of an obvious mechanical cause for suffocation and, second, the exclusion of fulminating infection. Sometimes, however, small children are found dead with a plastic bib firmly plastered over their faces. Here the diagnosis is seldom in doubt. The adhesive qualities of saliva and food remnants around the baby's mouth are usually blamed, but now the electrical properties of the bib itself may be called in question. Plastic bibs are obviously convenient, but they should be pinned to the baby's clothes to prevent disaster. As to the plastic bags, there is no question: small children should not be allowed to play with them. They are potentially lethal.

STEROIDS AND SURGERY

At first the administration of cortisone was restricted by its reputation for spreading infection and for delaying the healing of wounds. The drug was thus considered to be contraindicated in cases of tuberculosis, and was stopped if an infection occurred or surgery was required. It soon became clear that wound healing was hindered only if very large doses of steroids had been given, and a recent survey[1] has confirmed the clinical impression that healing is usually satisfactory after operations. Moreover, it is now common practice to prescribe steroids for overwhelming infections and even for tuberculosis, in addition, of course, to routine chemotherapeutic drugs.

The point nevertheless deserves emphasizing that patients receiving steroids require more, not less, cortisone if they are to survive the stress of an operation or infection. Death may occur even after minor surgical procedures or from trivial infections through failure to appreciate this, or because it had not been realized that the patient was receiving steroids.[2-7] The reason is that prolonged administration of steroids or corticotrophin leads to suppression of A.C.T.H. secretion by the pituitary and ultimately to adrenal atrophy. In such circumstances the adrenals are incapable of secreting the extra cortisol, which may be as much as 400 mg. a day,[8] required during stress. The extent of suppression is impossible to predict in the individual case. R. M. Salassa and his colleagues,[3] in a review of the available evidence, noted that as little as 100 mg. cortisone daily for four days could cause histological changes, and that a total dose of 2 g. was likely to result in adrenal atrophy. Perhaps of even greater significance is the fact that the adrenals may not be capable of responding to a major stress for as long as two years after cessation of long-term steroid therapy.

Unfortunately there is no practical procedure, short of measuring the output of 17-hydroxycorticosteroids in response to A.C.T.H., for determining adrenal function, and it is doubtful if any test would be possible in an emergency. It is therefore necessary to be clear about how to treat patients who are known to be receiving steroids or who have received treatment in the preceding two years. There is much to be said for such patients carrying a card similar to that issued to diabetics on insulin.[9 10] When a patient receiving steroids passes from the care of one doctor to another, it is important that information about the steroids should be communicated, and nurses should be carefully taught about the dangers of omitting them. Before operation or in the presence of infection 100–200 mg. of additional cortisone needs to be given by mouth or intramuscularly, and this dosage should be maintained for a few days until the danger of adrenal failure is past.[6 8] Thereafter the dosage is gradually reduced over a period of a week or ten days until the usual maintenance level is reached or the drug is stopped. Administration of A.C.T.H. is valueless, because it does not stimulate the suppressed adrenals for several days, and there are considerable variations both in potency of A.C.T.H. and in individual responsiveness. When there is a risk of adrenal failure—for example, in a patient who has not been given steroids because of the length of time that has elapsed since he last received them—it is worth keeping a careful watch for signs of it; they include anorexia, nausea, vomiting, hiccup, fever, weakness, tachycardia, and hypotension.[11] If any of these occur and there is a reasonable suspicion that adrenal hypofunction is the cause, 100 mg. hydrocortisone should be given intravenously in 500 ml. of 5% glucose, up to a total of 400 mg. in the 24 hours. If hypotension does not respond promptly, 2–4 mg.

[1] Popert, A. J., and Davis, P. S., *Lancet*, 1958, **1**, 21.
[2] Fraser, C. G., Prouss, F. S., and Bigford, W. D., *J. Amer. med. Ass.*, 1952, **149**, 1542.
[3] Salassa, R. M., Bennett, W. A., Keating, F. R., Jr., and Sprague, R. G., ibid., 1953, **152**, 1509.
[4] Lewis, L., Robinson, R. F., Yee, J., Hacker, L. A., and Eisen, G., *Ann. intern. Med.*, 1953, **39**, 116.
[5] Allanby, K. D., *Lancet*, 1957, **1**, 1104.
[6] Slaney, G., and Brooke, B. N., ibid., 1957, **1**, 1167.
[7] Richardson, A. T., and Hess, E. V., *Brit. med. J.*, 1957, **2**, 998.
[8] Bayliss, R. I. S., ibid., 1958, **2**, 935.
[9] Slocumb, C. H., Polley, H. F., Ward, L. E., and Hench, P. S., *Ann. intern. Med.*, 1957, **46**, 86.
[10] Welbourn, R. B., *Irish J. med. Sci.*, 1957, **6S.**, 401.
[11] Ward, L. E., Polley, H. F., Slocumb, C. H., and Hench, P. S., *J. Amer. med. Ass.*, 1953, **152**, 119.

noradrenaline may be added to the infusion. Infection and complications following surgery may be masked by steroid therapy, and patients with infections may require large doses of antibiotics as well as extra cortisone.

REDUNDANT CONSULTANTS

The way is now open for belated justice to be accorded to Mr. A. H. Barber, the Oldham gynaecologist whom the Manchester Regional Hospital Board wrongfully dismissed in 1952. The Minister of Health has amended the National Health Service (Appointment of Specialists) Regulations, so that now regional boards may offer employment to redundant consultants and S.H.M.O.s without throwing the posts open to competition. The new regulations[1] (see *Supplement* at p. 257) came into force on May 27, and apply to Scotland as well as to England and Wales. The immediate effect[2] of this welcome news has been for the Manchester Regional Hospital Board to defer the filling of the vacant consultant post with the Ashton-under-Lyne, Hyde, and Glossop Group of Hospitals, for which Mr. Barber had applied but failed to be short-listed by the advisory appointments committee.[3] This was the second consultant post in the board's area for which Mr. Barber had applied unsuccessfully[4] since the Minister[5]—and the board[6]—had accepted a "moral obligation" to assist him. After a seven-year battle, which has included a successful High Court action,[7] repeated pressure on the Ministry by the B.M.A. and the Joint Consultants Committee, a campaign in the lay press, and questions in both Houses of Parliament, bureaucratic rigidity and inertia stand exposed, confounded, and defeated. It only remains now for the Manchester Board swiftly to find Mr. Barber suitable work.

The new regulations go much further than making justice for one man administratively possible. Clause 16 of the Terms and Conditions of Service of Hospital Medical Staff is the only safeguard for consultants and S.H.M.O.s against unfair dismissal. It is written into their contracts with regional boards. But if, as we said earlier in these columns,[8] the "moral obligation" to assist consultants redundant through no fault of their own could not be enforced, what was their security worth? For long enough the B.M.A. and the Joint Consultants Committee have been hammering at successive Ministers of Health to give substance to their paternal assurances, to give teeth to their undertaking of moral obligation. The new regulations appear to do this. "When as a result of contraction of work or of local reorganization," states the Ministry's explanatory memorandum[9] to hospital authorities, "it becomes or has become necessary for a board to terminate the appointment of a consultant or a senior hospital medical or dental officer, the board should first consider whether they can vary his contract and offer him alternative employment. An appointment offered in these circumstances need not necessarily be in the same specialty as the officer's existing post, provided that he has the necessary qualifications for the new post." If the board itself has no post to offer, and the officer assents, the board should notify all other boards. This goes a long way to remedying a serious defect in the terms of employment in the hospital service, and it has taken the Minister far too long to put a wrong right.

[1] *The National Health Service (Appointment of Specialists) Amendment Regulations, 1959*. S.I. No. 909, 1959.
[2] *The Times*, May 27, 1959.
[3] *Brit. med. J.*, 1959, **1**, 1310.
[4] Ibid., 1959, **1**, 1253.
[5] Ibid., 1958, **2**, 171.
[6] *Hansard*, December 8, 1958.
[7] *Brit. med. J.*, 1957, **2**, 1552.
[8] Ibid., 1959, **1**, 702.
[9] H.M. (59) 57.

DR. ELLIOTT JOSLIN

To-day Dr. Joslin is 90. We hail him as "dean of the American medical profession," in the apt phrase of the editor of the *New England Journal of Medicine*, whose birthday tribute we print elsewhere (p. 1468); as pioneer and great authority on the care of the diabetic; and, with special pleasure, as a most distinguished Foreign Corresponding Member of the B.M.A. Whether or not of the fortunate many treated personally by him, diabetics in the United States owe Dr. Joslin an incalculable debt of gratitude. His life was given to their service. Beginning in 1893 with his first diabetic patient, as Dr. Garland reminds us, Joslin has remained in the forefront of the battle; he was the first to use insulin in the United States, and he still goes on. To doctors everywhere he has given the distilled wisdom of his experience: by example; by his teaching at the bedside, in consultation, and at the rostrum; and by his writings. By happy coincidence we are able to review this week the tenth edition of his famous textbook, first published in 1916, *The Treatment of Diabetes*. And it was not so very long ago that we printed in our opening pages his papers on "A Half-century's Experience in Diabetes Mellitus"[1] and "Lessons for Future Treatment from 472 Fatalities in Diabetic Children."[2]

This is not the place or occasion to list the many honours, both domestic and international, that have rightly come his way—nor, we are sure, would he like us to do so. Rather let us picture Dr. Joslin as a young British physician found him recently, when visiting the Deaconess Hospital in Boston. "I met him at the Deaconess," he tells us, "at the ungodly hour of eight o'clock in the morning, when I'm sure that he, with all his weight of years, was much more *compos mentis* than I. As far as I know, this was a daily performance, when all the team reviewed the patients currently in the wards. He sat alone in the front row, thin and old and silent, but every now and then added some pithy comment showing he was still very much on the ball. Afterwards I was shown round the clinic by his son." We salute Dr. Joslin at his happy vigil.

[1] Joslin, E. P., *Brit. med. J.*, 1950, **1**, 1095.
[2] —— and Wilson, J. L., ibid., 1950, **2**, 1294.

Drug Treatment of Disease

TREATMENT OF DIABETES MELLITUS

HYPOGLYCAEMIC AGENTS OTHER THAN INSULIN

BY

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Less than 50% of patients with diabetes mellitus need insulin for the control of their condition. Evidence is accumulating to show that the remainder have no true deficiency of this hormone. It has long been recognized on clinical grounds that diabetics may be divided into two groups: on the one hand the thin patients who quickly become ketotic in the absence of insulin treatment, and on the other those who are or have been obese and, although they have hyperglycaemia, show no tendency to develop ketosis. It has been suggested that the former are insulin-deficient whereas the latter have become resistant to the action of insulin. Confirmation of this differentiation has been obtained from estimations of plasma-insulin activity and from study of the amount of insulin that can be extracted from the pancreas removed at necropsy in suitable cases.

Dietary Treatment of Diabetes Mellitus

Insulin resistance of the overweight diabetic is apparently related to the obesity, and if reduction in weight can be achieved by a suitable diet low in calories and carbohydrates the symptoms usually disappear and blood-sugar levels often return to normal. The diets used provide 1,000 to 1,750 calories a day and contain 100 to 120 g. carbohydrate. Some patients co-operate well in their treatment, but many find it difficult to keep to a restricted diet. This may be for economic reasons, because diets of this type are expensive if they are to be satisfying. In other cases the patients' personalities or environment may make it difficult for them to keep to the prescribed diet. In selected cases drugs like dexamphetamine or "preludin" (phenmetrazine hydrochloride) may help the patient to control the appetite; thyroid preparations cannot be recommended for weight reduction. In most cases the symptoms improve within a week or two of starting the diet, and as the weight comes down the post-prandial or random blood sugar estimation will be less than 200 mg./100 ml. Despite this the diabetes is not cured, the glucose tolerance curve usually remains of a diabetic type, though the blood-sugar levels will be lower than those obtained before treatment started; if the patient's weight goes up again overt diabetes will reappear.

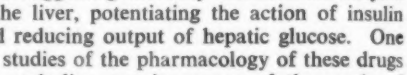
About 15% of these obese diabetics will continue to have a high blood sugar despite getting their weight down to an average level or even below. These patients seldom have any diabetic symptoms, the only abnormalities being glycosuria and raised blood-sugar. Unfortunately there is evidence to suggest that this hyperglycaemia may lead to the development of diabetic complications like retinitis, impaired renal function, or arterial disease. Until recently the only way to lower the blood sugar was by giving insulin, and it was not easy to explain to a symptomless middle-aged or elderly diabetic that daily injections were necessary. It is in just this group of patients that tablets of the hypoglycaemic sulphonamide derivatives are indicated.

Hypoglycaemic Sulphonamide Derivatives

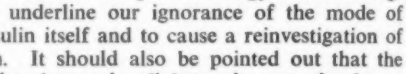
These compounds lower the blood sugar in normal subjects and in some diabetics. How they do it is uncertain, but they are not to be regarded as "oral insulin preparations," because unlike insulin they have no direct effect on utilization of carbohydrate by the peripheral tissues. It has been established that they lower the blood sugar only if the patient's pancreas is capable of secreting some insulin, and one way in which they act is apparently to increase the pancreatic output of insulin (Loubatières, 1957). There is also some evidence suggesting that they influence the enzyme systems of the liver, potentiating the action of insulin on them and reducing output of hepatic glucose. One result of the studies of the pharmacology of these drugs has been to underline our ignorance of the mode of action of insulin itself and to cause a reinvestigation of this problem. It should also be pointed out that the metabolic disturbance in diabetes is not simply an increase of sugar in the blood. These drugs will lower the blood sugar, but there is no evidence that they will correct the other biochemical abnormalities in diabetes mellitus. It is appropriate therefore to refer to them as hypoglycaemic drugs but not to describe them as antidiabetic.

There are three compounds to be considered:

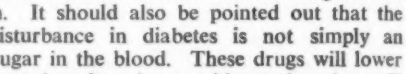
Carbutamide



Tolbutamide



Chlorpropamide



Carbutamide.—This was the first of the hypoglycaemic sulphonamide derivatives to be given extensive trial. Its excretion is slow, so that satisfactory blood levels were achieved with doses of about 1 g. a day, and a single daily dose was all that was needed. Unfortunately, however, a number of serious and some fatal toxic reactions occurred. The commonest was a sulphonamide sensitivity reaction with widespread arterial damage; a few patients developed agranulocytosis, and thrombocytopenia was not uncommon (Kirtley, 1957). Because of these toxic effects this drug is no longer made in this country or in the United States.

Tolbutamide.—This compound is the one most widely used at the present time. The *p*-amino group of carbutamide has been replaced by a methyl group with loss of antibacterial action and marked reduction of toxicity. Tolbutamide is excreted more quickly than carbutamide and must be given in divided doses two or three times a day (Baird and Duncan, 1957). The total daily dose is usually 1–3 g. Side-effects include indigestion, occasionally pain suggestive of peptic ulcer, and irritating rashes.

Chlorpropamide.—This is a recent addition to the oral hypoglycaemic agents and is now generally available in this country. It is excreted very slowly and therefore need be given only once a day. The blood levels obtained are higher than those of tolbutamide and the hypoglycaemic action consequently greater. The usual daily dose is 0.25 to 0.5 g. a day. If larger doses are given hypoglycaemic attacks may be produced and some peculiar neuropsychiatric side-effects may result—vertigo, confusion, and so on (Murray *et al.*, 1958). A few cases have been reported of cholangiolitic jaundice after small doses of chlorpropamide. The clinical and pathological changes are similar to those seen in chlorpromazine jaundice.

Tolbutamide Therapy

Patients suitable for tolbutamide therapy are those who develop diabetes in middle age or later. It should not be given to patients who have had marked ketonuria or diabetic ketosis. Most of the suitable patients belong to the group of obese diabetics, and before tolbutamide is given body weight should be reduced by a suitable low-calorie, restricted-carbohydrate diet to within 10% of the average weight for a person of similar age and height (Kemsley, 1952). If, despite weight reduction, glycosuria and hyperglycaemia persist, tolbutamide may be started. The initial dose should be 0.5 g. three times a day, and if necessary it may be increased to 0.5 g. four times a day or 1.0 g. three times a day. The response to tolbutamide may be immediate or delayed, and, because of the delayed type of response, trial of tolbutamide therapy should be continued for four to eight weeks before it is abandoned as unsuccessful. It had been hoped that a one-day test with a large dose of tolbutamide and serial blood-sugar estimations would make it possible to decide which cases were suitable for tolbutamide therapy; in practice, however, it has proved unsatisfactory and therapeutic trial is needed (Dolger, 1956). If there is a good response on 0.5 g. three times a day, it may be possible to reduce the dose to 0.5 g. twice a day or 0.25 g. twice a day. Dietary control must be continued, but, if the patient is underweight and the blood-sugar levels are satisfactory on tolbutamide, gradual increase of calorie and carbohydrate intake may be permitted.

Before tolbutamide became available diabetics of the type considered in the last paragraph had to be given insulin to control their hyperglycaemia, and the question of changing to tolbutamide now arises. It is often difficult to recognize the patients who will be suitable for tolbutamide therapy as opposed to the insulin-deficient type who will become ketotic if treatment with insulin is stopped. If the dose of insulin is more than 30 units per day satisfactory control with tolbutamide is unlikely to be achieved. Patients who are overweight should have their obesity corrected by adjustment of the diet and reduction of the dose of insulin before the change is attempted.

There are various methods of effecting the change of treatment. The simplest is to reduce the dose of insulin over a period of a few days, and when hyperglycaemia or glycosuria is observed to start the tolbutamide at 0.5 g. three times a day. This may be necessary before insulin is stopped or a few days or weeks after stopping it. Some patients are found to remain well controlled without insulin; in other words, they were taking it unnecessarily and of course they do not need tolbutamide either. While the insulin dose is being reduced and for a few days after it is stopped the urine must be tested daily for ketone bodies; if they are found the patient is unsuitable for tolbutamide therapy and insulin must be started again straight away. During this period the doctor should see his patient every day, facilities must be available for getting blood-sugar estimations done at short notice, and in some cases it is advisable for the patient to be admitted to hospital.

Tolbutamide is a comparatively new drug, and all patients on it must be seen regularly, initially at weekly intervals and when well controlled at least every four weeks. Check should be kept on the urine tests and weight; if possible, the blood sugar should be estimated periodically, because many of these patients have a high renal threshold and a high blood sugar without glycosuria. If a skin rash develops, treatment with tolbutamide usually has to be abandoned. Indigestion is sometimes troublesome; it may be minimized by giving the tablets after meals and prescribing an antacid; occasionally it necessitates stopping the treatment. Some patients seem to become resistant to the action of tolbutamide after they have been taking it for 6–18 months. This may result from laxity in diet, when it is associated with an increase of body weight; but in some there is genuine acquired resistance, with heavy glycosuria, weight loss, and often ketonuria. If this happens tolbutamide must be stopped and insulin therapy started.

Chlorpropamide Therapy

The indications for chlorpropamide are similar to those for tolbutamide, but the initial dose should be 0.25–0.5 g. a day. In small elderly subjects it should not exceed 0.25 g. a day. The dose should be reduced as soon as possible to a maintenance level which may be as low as 100 mg. a day. Because of the high blood levels achieved it is more potent as a hypoglycaemic agent than tolbutamide, and it may work where the latter fails to produce an adequate reduction of blood sugar. On the other hand, it is possible to produce genuine hypoglycaemic attacks with it. Skin sensitization has been reported, and the incidence of jaundice after its use cannot yet be assessed.

Phenethyldiguanide (D.B.I.)

This is an oral hypoglycaemic agent unrelated to the sulphonamide derivatives but in some ways resembling "synthalin," which was used in the treatment of diabetes in the 1920s and abandoned because of toxic effects on the liver (Graham and Linder, 1928). D.B.I. is active in the absence of insulin and has been given with some success to juvenile diabetics (Krall and Camerini-Davalos, 1958). It seems to reduce the blood sugar by increasing anaerobic glycolysis. In practice it has been found that at least half the patients get gastro-intestinal side-effects with therapeutic doses, and for this reason it seems unlikely that D.B.I. will be widely used in the treatment of diabetes (Hall *et al.*, 1958).

Recent reports of a new diguanide, the dimethyl compound, suggest that it may be as effective as D.B.I. although a larger dose is needed, and that it is much less likely to upset the gastro-intestinal tract (Azérad and Lubetski, 1959).

Other Hypoglycaemic Agents

Many other compounds have been used in the treatment of diabetes. There are numerous herbal and vegetable remedies, but they do not seem to have a

consistent hypoglycaemic action (Hugh-Jones, 1955; Sepaha and Bose, 1956). Oestrogenic hormones have been given for diabetes developing at puberty and for the diabetes found in post-menopausal women (Gessler *et al.*, 1939). Dimercaprol has been shown to reduce the blood sugar in a few diabetics, but it is unlikely that it will be used in treatment (Butterfield and Thompson, 1957). The salicylate drugs are of considerable interest. They lower the blood sugar in some diabetics (Reid *et al.*, 1957) and also appear to enhance the hypoglycaemic action of the sulphonamide derivatives (Stowers *et al.*, 1958).

REFERENCES

Azérad, E., and Lubetzki, J. (1959). *Bull. Soc. méd. Hôp. Paris*, **75**, 132.
Baird, J. D., and Duncan, L. J. P. (1957). *Scot. med. J.*, **2**, 341.
Butterfield, W. J. H., and Thompson, R. H. S. (1957). *Clin. Sci.*, **16**, 679.
Dolger, H. (1956). *Metabolism*, **5**, 947.
Gessler, C. J., Halsted, J. A., and Stetson, R. P. (1939). *J. clin. Invest.*, **18**, 715.
Graham, G., and Linder, G. C. (1928). *Quart. J. Med.*, **21**, 509.
Hall, G. H., Crowley, M. F., and Bloom, A. (1958). *Brit. med. J.*, **2**, 71.
Hugh-Jones, P. (1955). *Lancet*, **2**, 891.
Kemsley, W. F. F. (1952). *Ann. Eugen. (Lond.)*, **16**, 316.
Kirtley, W. R. (1957). *Diabetes*, **6**, 72.
Krall, L. P., and Camerini-Davalos, R. (1958). *Arch. intern. Med.*, **102**, 25.
Loubatières, A. (1957). *Diabetes*, **6**, 408.
Murray, I., Riddell, M. J., and Wang, I. (1958). *Lancet*, **2**, 553.
Reid, J., Macdougall, A. I., and Andrews, M. M. (1957). *Brit. med. J.*, **2**, 1071.
Sepaha, G. C., and Bose, S. N. (1956). *J. Indian med. Ass.*, **27**, 388.
Stowers, J. M., Hunter, R. B., and Constable, L. W. (1958). At the New York Academy of Sciences Conference on Chlorpropamide and Diabetes Mellitus.

DR. ELLIOTT JOSLIN: A BIRTHDAY TRIBUTE

Written at the special invitation of the B.M.J. by

JOSEPH GARLAND, M.D.

Editor, "New England Journal of Medicine"

Elliott Proctor Joslin, dean of the American medical profession and authority extraordinary on diabetes to a considerable proportion of the civilized world, will celebrate his ninetieth birthday on June 6. That is, his devoted friends, relatives, associates, and admirers will presumably press some sort of a celebration on him; he will probably spend at least part of the day in his office, attending to business as usual.

Dr. Joslin was born these fourscore and ten years ago in the town of Oxford, Massachusetts. As a boy, it has been reported, he spent his spare hours working in his father's shoe factory putting laces into shoes at six cents per 60 pairs. The inflationary sums thus amassed were not spent riotously, however; his father insisted that they be put into the savings bank, where they still remain. Frugal in his personal life, Dr. Joslin is such a ready giver in good causes that his friends fear his coming to want if old age ever overtakes him. Perhaps the interest on the pennies in the bank will yet serve to rescue him.

From the academy in the neighbouring town of Leicester Elliott went to Yale College and then to Harvard Medical School, then to the Massachusetts General Hospital for an internship. It was here, in 1893, as a student, that he acquired his interest in diabetes through his care of Mary Higgins, the first case in his series of over 50,000 diabetic patients. A spare person, one of Dr. Joslin's aphorisms is that people who run 10 to the ton are most likely to acquire diabetes. Dr. Joslin was one of the first to recognize the achievement of Banting and Best in Macleod's Canadian laboratory in 1922, and he was the first to use insulin in his own country.

Years ago he started the custom of giving a bronze medal to each of his diabetic patients who exceeded the normal life expectancy (there have been over 2,000 of them) and a gold medal to those who more than doubled it. A gold medal recipient was George F. Baker, then president of the First National Bank of New York, whose award was bread upon the waters, for he eventually left a quarter million dollars for the Baker Diabetic Clinic at the New England Deaconess Hospital in Boston. The frieze by Malvina Hoffman on the new Joslin Clinic building opened last year at the Deaconess Hospital, representing the history of medicine, starts with Imhotep and ends with the late George Richards Minot, the diabetic physician of Boston who received the Nobel Prize for his part in discovering the liver treatment for pernicious anaemia. He was another of the 50,000 who owed to Dr. Joslin and his associates the renewed capacity to carry on.

YOU MAY MEET A CANADIAN DOCTOR

BY

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A wave of Canadian doctors will sweep into Britain in July, ostensibly for the B.M.A.–C.M.A. Convention in Edinburgh. Actually this will be a convenient tax-deductible excuse to visit Europe. Over a thousand doctors are expected to cross the Atlantic for this conclave: a week later they will disperse into the small towns, villages, and cities of Britain, enthusiastically sniffing out "the real set-up" with trained curiosity, anxious to meet and discourse with their British colleagues. This is where you may come across one. Let me prepare you for what to expect, so that when the encounter takes place you will be able to get straight to the interesting points of reciprocal analysis without precious minutes being wasted on trivialities.

First, the chances are considerable that your new-found friend will not be Canadian-born, especially because of the extra appeal this trip will have for emigrant Europeans. He may well speak guid Scots or cultured English, even guttural German or quixotic French. Don't be put off by this initial surprise: he is still a Canadian. His clothes will establish it. It will be summer-time, and he will be wearing a brilliant sports shirt done up at the neck, with a jacket over it. Having just come from Edinburgh, he'll wear a jaunty tartan cap. There will be a movie-camera slung over his shoulder, and, if he is a surgeon, a cigar in his mouth. But he won't be bombastic in the way his garb suggests. He will be rather quiet, shy, and anxious not to offend. Such is the curious Canadian blend.

Secondly, he will be, to your way of thinking, wealthy. To make this visit with his wife this year will mean that something he wanted (or she did) has had to be postponed twelve months: maybe it was the new Mercedes-Benz for which he was going to trade in his 200-h.p. American car; perhaps it was the stereophonic hi-fi equipment they had been looking forward to, or the swimming-pool in his garden, or the 25-foot cabin cruiser. At any rate he will have given something up, and he will tell you about it in all seriousness. Please don't laugh at him. It was a hard decision for him to make. If you can help, through your hospitality, to justify it for him (and you can, more than the Houses of Parliament, French brandy, or even St. Peter's, Rome), you are doing him a service he will never forget.

Canadian Demand for Medical Freedom

You will inevitably begin to talk about medical practice. He may be a specialist, but this doesn't mean he's a consultant. In some cities there are more specialists than G.P.s, but probably only one-tenth of these are full-time consultants; the rest treat any patient or any disease that comes their way, referring them to other specialists only if the condition is serious, so far removed from their field that they are quite hazy about treatment, or likely to require house-calls. In this last circumstance they may, in desperation, refer to a G.P.

If you run into a Canadian G.P. prodding about the Welsh hills, or gazing intently at art in the Tate Gallery, and you fall into a chat with him, don't be surprised when he tells you about his hysterectomy mortality rate, his programme for home anticoagulant therapy with daily prothrombin times estimated by his own laboratory technician, or his daily hospital round in the medical, surgical, obstetric, and paediatric wards. After several such conversations you will wonder who does the general practice and who the specialist work in Canada. Do not be deceived by this strange enigma. The Canadian public demand this state of freedom in their medical affairs, and through it all their medical treatment is equal to that anywhere in the world.

You may feel proudly constrained to show him your surgery, and casually to run your finger down yesterday's list of patients. Your pride will be vindicated: he will be speechlessly impressed. He will wonder how you can possibly get by without three examining-rooms or relayed soft music in the waiting-room. You must be a real topnotch dedicated doctor to have that staggering daily list. Remember that he never sees a patient without appointment, and almost everyone strips at least to the waist at each visit. Remember that each visit costs the patient, directly or through insurance, about 30s., with twice this for house-calls. Remember his office (surgery) closes every night by 5.30 p.m. so that his £20 a week nurse can go home. He plays golf once a week and takes alternate week-ends off, if he has an arrangement with another practitioner. He may give the impression of being overpaid, underworked by your standards, and possessed of a conceited megalomania if you break off your casual discussion at this stage.

His Frustrations

To dispel this impression, simply scratch below the epithelium, and you will find his subcuticular frustrations are equivalent to your own. He has a fiercer problem of competition than you have, if he is in city or suburban practice. The doctor next door went broke last week: a personality problem was your friend's diagnosis. Could it happen to him, he wonders? The dentist downstairs has installed T.V. in his waiting-room. Should he? Dr. Complex down the road, his rival G.P., has a new electrocardiograph. Hadn't he better get one? Dr. Social has just joined the country club: maybe he ought to join the yachting fraternity. And so on, through cars, houses, and all the other hideous hallmarks of prosperity. He can't escape it.

His patients are more medicine-conscious, more aware of medical shortcomings, than yours are. They are quicker in criticism, slower in faith than yours. Possibly 5% are medical shoppers, using their insurance schemes and their absolute freedom of choice to try out all the doctors in the district with their symptoms and then compare diagnoses. More is expected of the family doctor in Canada than in Britain: unless he is adequately skilled in all but the most highly specialized procedures, his reputation and practice and income remain proportionately diminished. Every time he refers a patient, sneaking doubt assails that patient's mind, and so he may lose him to a "broader" practitioner. Over and above all, he has, like you, a day largely made up of minor upper respiratory infections which he is required to treat with, I venture to say, greater self-disciplined respect than you do.

Conclusion

Consider all these things when you meet your Canadian colleague. Never feel ashamed when confronted by his rented Jaguar or invitation to dine at

his Mayfair hotel. If you show him the volume of your work, he will reel back in genuine admiration. Your home may seem modest to you in comparison with his, but tea and crumpets there will be the most treasured memory of his visit. Whether or not he is of British origin, he has come to Britain because Britain was worth coming upwards of six thousand miles to see. He will probably come back to Canada saying, as a leading Canadian magazine columnist did recently, "They've got something there we haven't."

BRITISH ORTHOPAEDIC ASSOCIATION

SLIPPED UPPER FEMORAL EPIPHYSIS

[FROM A SPECIAL CORRESPONDENT]

The Spring Meeting of the British Orthopaedic Association was held in Torquay and Exeter under the presidency of Mr. NORMAN CAPENER from April 30 to May 2. This meeting was held in conjunction with the French and Belgian Orthopaedic Societies. One of the main items was a symposium on slipped upper femoral epiphysis. This is a subject on which opinions still differ. The nature of the deformity—backward and downward displacement of the femoral head in relation to the neck—has long been appreciated, but its cause is not really understood, though some connexion with endocrine disturbance is generally conceded.

Cause of the Displacement

Mr. A. M. RENNIE (Aberdeen) presented a most interesting theory of the aetiology of the slip, basing his observations on a series of 63 patients whom he had studied over a period of twelve years. In 32 hips in which the deformity had developed gradually the anterior surface of the femoral neck was materially longer than the posterior surface, which resulted in a posterior tilt averaging 31.5 degrees, as against the normal 10 degrees. Among these patients there were also five instances of premature fusion of epiphyses unrelated to the hips. From these findings he suggested that in these patients the epiphysial plates were unduly sensitive to compression, and that because of the rather peculiar mechanics of the hip the posterior part of the upper femoral plate was subjected to compression strains during external rotation. This resulted in slowing of the growth of this part of the plate and hence an increasing backward tilt, which in due course reached pathological proportions, when the slip occurred.

Dr. ROBERT SŒUR (Brussels) supported the view that the slip was due to mechanical factors, but considered that the compression occurred on the lower part of the plate. He demonstrated that in this region the bone structure was sclerotic, whereas in the upper part of the plate, where there was no compression, the bone structure was porotic.

In the subsequent discussion Professor B. MCFARLAND (Liverpool) said that if this theory of the aetiology was correct it would be logical for everyone to have a slipped upper femoral epiphysis instead of it being an uncommon condition. Professor R. I. HARRIS (Toronto) thought the examples shown were those in which some degree of slipping had already occurred rather than that any growth imbalance was present. He considered that the cause of slipping was an endocrine imbalance. He showed slides demonstrating the fact that in rats treated with excess of growth hormone the epiphysial plate became widened and therefore more susceptible to minor traumata.

Conservative Treatment

The treatment of the condition has changed considerably during the past fifteen years. Before that time only the most gentle forms of manipulation combined with traction were permitted, and this was followed by a period of immobilization until the epiphysial plate had closed. After the second world war surgeons became more venturesome in their approach, using internal fixation more and more and combining this with manipulative reduction when necessary or even open reduction or osteotomy of the neck where this was not possible. More recently the pendulum has swung back, and this conference emphasized just how much. The problems in treatment have always been the correction of the deformity without endangering the vascularity of the head, and early closure of the plate to prevent further displacement; all speakers were unanimous in their view that no treatment must be considered which would endanger the femoral head.

Dr. PIERRE PETIT (Paris) advocated the purely conservative approach whenever possible. He had treated 25 hips in which the displacement was gradual by immobilization without any attempt at reduction—14 in plaster spicas, 7 with continuous traction, and 4 with bed rest only. Time would be wasted unnecessarily if immobilization were continued until the plate had closed, and he thought it safe to allow movement, and even weight-bearing, once the bone structure on either side of the plate had returned to normal. This method resulted in 21 good hips, 3 fair, and 1 bad. If the subsequent deformity led to disability it should be corrected by subtrochanteric osteotomy, he said.

When the slip was acute, he advocated manipulative reduction, but this did not give such good results.

A somewhat similar approach was advocated by Mr. ROWLAND HUGHES (Oswestry), who based his views on 72 hips, of which 46 had been treated conservatively. In any hip in which the deformity was acceptable the position should be stabilized by internal fixation, which he considered gave good results. If the deformity was more extreme he advised mobile traction with internal rotation, finding that any rigid fixation led to subsequent stiffness and that those immobilized in plaster were subject to further displacement. Manipulation should be avoided because, in his experience, it produced only one satisfactory result out of 6. None of the methods he had used materially improved the deformity; if necessary, deformity should be corrected by subtrochanteric osteotomy at a later date.

Multiple Pinning

Mr. P. H. NEWMAN (London) also discussed treatment. For cases in which the position was acceptable (65%) he advocated stabilization by internal fixation, preferring multiple pins to one big nail. He obtained excellent results by this method. For cases in which the position was unacceptable but in which it could be corrected (10%), he suggested gentle manipulation under anaesthesia and fixation by pinning. This had given excellent results in his hands. Finally, there were those where the position was both unacceptable and uncorrectable by manipulation. For them he thought transcervical osteotomy too risky, and preferred subtrochanteric osteotomy later on.

Mr. F. C. DURBIN (Exeter) supported Mr. Newman's views. On the basis of a follow-up of 81 hips in 63 patients, he was in no doubt that operative fixation with multiple pins was better than conservative treatment, which often involved a long period of invalidism. He believed that in hips treated conservatively weight-bearing should be delayed until the epiphysial plate had closed. Out of 19 hips treated conservatively, slipping had recurred in three. He also emphasized the great importance of early diagnosis. Where the slip was only minor the results of treatment were good, but where the degree of displacement was such as to necessitate correction—which he advised should be done by gentle manipulation under anaesthesia—the results became less satisfactory; if the degree of slip exceeded half the diameter he considered correction necessary to avoid otherwise inevitable osteoarthritis later. In agreement with all the other speakers he advised that if these manœuvres failed the deformity should be corrected by subtrochanteric osteotomy, angled into 45 degrees of abduction to prevent contact of the raw bone between the neck and epiphysis with the acetabular rim.

Bone Grafting

Dr. JEAN JUDET (Paris) was more radical in approach. He recognized four stages: first, where the displacement was minimal or nil; second, where the contact between head and neck of femur was less than two-thirds; third, where the displacement was severe, making an angle of 35 degrees to 70 degrees; and, fourth, where the displacement resembled a fracture of the femoral neck. Treatment had depended on this staging in the 85 hips which he and his collaborators had reviewed. In stage I, where the slip was minimal, he advised internal fixation and preferred to use a bone graft to ensure fusion of the plate as soon as possible. In stage II the principles were the same: reduction was unnecessary, but some form of internal fixation was used; and again the bone graft was preferred, although good results had been obtained with metal. In 35 hips at this stage they had had only two bad results. For stage III cases they had corrected the deformity by osteotomy of the neck and internal fixation, but the results had been bad: out of 21 hips so treated, 17 were unsatisfactory. In stage IV Dr. Judet advocated closed manipulative reduction and internal fixation to ensure fusion of the epiphysial plate.

Avascular Necrosis

All speakers were agreed that any procedure which endangered the blood supply of the femoral head must be avoided even if this involved accepting deformity, which must later be corrected by osteotomy. Mr. H. G. LOWE (Cardiff) said he had found 20 cases of avascular necrosis in 100 hips he had investigated. They fell into two groups: those showing density of the femoral head but with a good joint space, and those with acute necrosis of the articular cartilage and loss of joint space. The second group was much the larger and much the more serious. Increased sclerosis was seen in only 5 hips, and all of them did well, but in the 15 hips with necrosis of the articular cartilage the prognosis was bad. Four such hips which came to arthrodesis showed at operation extensive necrosis of both the femoral and acetabular articular cartilage. This suggested other factors besides avascular necrosis of the head of the femur, and he thought that factors which might interfere with the normal secretion of synovial fluid, such as excessive traction producing subluxation, or prolonged immobilization, might play a part. But two hips had shown changes before treatment began, and in two other cases the good hip developed necrosis while the other hip was under treatment.

In the discussion Professor J. TRUETA (Oxford) showed slides of femoral heads in which the blood vessels had been injected. These showed the lateral epiphysial vessels which form the main blood supply to the head and also indicated how vulnerable they would be to damage at operation on this part of the femur. He hoped that cervical osteotomy would be abandoned.

Professor MCFARLAND (Liverpool) said that the important points to consider were how great was the slip and how rapidly it had occurred. If it had happened acutely the epiphysis might already be damaged, but if the slip was gradual its blood supply would be intact, but might well be damaged by treatment. In each type the treatment and prognosis were different.

Diagnosis of Necrosis

At this meeting there were five travelling fellows from North America and Canada as guests of the British Orthopaedic Association. One of these, Dr. J. S. MILES, of Denver, presented a paper on the diagnosis of avascular necrosis of the head of the femur in subcapital fractures of the neck by testing the intramedullary pressures.

It is important to diagnose as early as possible the presence of avascularity in these cases so that an accurate prognosis can be made. If the diagnosis is left to serial radiography it may be many months or longer before it can be seen with certainty. Many methods have been tried to hurry the

(*Continued at foot of next column*)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Riston (Imperial Chemical Industries).
Spontin (Abbott Laboratories).

These are preparations of ristocetin, an antibiotic which has two components designated ristocetin A and ristocetin B. The latter is more active than the former both *in vitro* and *in vivo*. The two antibiotics are additive in effect. Bacterial resistance, especially by the *Staphylococcus aureus*, does not develop rapidly, and they are bactericidal for this micro-organism. The antibiotic is available in phials of 500 mg. to hospitals only.

Ristocetin is primarily indicated in the treatment of hospital-acquired infection with staphylococci, which are usually resistant to the more commonly administered antibiotics, and should be reserved at present for this purpose. Treatment is best given by intravenous injection, because this antibiotic is poorly absorbed from the gastro-intestinal tract. Exact dosage schedules have not been worked out, but daily totals range between 1.5 and 6 g., and a total course of treatment averages 35 to 40 g. Susceptible infections should be controlled by 10 to 14 days' treatment.

In high dosage the antibiotic has caused leucopenia. Skin rashes may arise, but severe anaphylactoid reactions have not so far been reported. Mild phlebothrombosis may appear at the site of injections, but can be avoided by varying the site.

Hospital price: riston and spontin, one 500-mg. phial, 32s.

Stemetil (May and Baker).—This is prochlorperazine maleate, or 2-chloro-10[3-(4-methylpiperazin-1-yl)propyl] phenothiazine dimaleate. It is marketed in 5-mg. tablets and 25-mg. suppositories. It was first widely used for its associated sedative and antiemetic effects in motion sickness, and was found to be of much benefit. Later it was tried in patients with Ménière's syndrome and other types of aural vertigo, and more recently in cases of migraine. It may be given continually as a sedative (up to 20 mg. two or three times a day) to try to prevent vertigo or migraine, or at the time of the attack, in similar doses, to cut it short. Continued treatment with large doses causes tremors and a parkinsonian syndrome (like that seen with related tranquillizers), but these symptoms subside on withdrawing the drug or on giving promethazine. It has become usual therefore to give 10 mg. twice or thrice a day for prolonged sedation, or to give larger doses occasionally if used as a hypnotic, as in psychiatric practice. So far no serious complications of treatment with stemetil have been reported.

N.H.S. basic price: tabs. 5 mg., 250 for 30s. 10d.; tabs. 25 mg., 500 for 150s.; suppositories, 5 mg., 5 for 4s.; 25 mg., 5 for 5s. 6d.; amps. (1.25%), 10×1 ml., for 5s. 6d.; 10×2 ml., for 9s. 2d.

(*Continued from preceding column*)

diagnosis, such as needle biopsy, radioactive isotopes, and dyes, only to mention a few. Dr. Miles suggests that, if the blood supply to a bone is cut off or reduced, the intramedullary pressure, which is normally about 20 mm. Hg, will be reduced. To ascertain this he introduces a trocar and cannula into the femoral head under *x*-ray control. In the normal hip, the pressure as read off on a manometer rises to 20 mm. Hg, but when a fracture is present it is lower. If there is any doubt about this a pressor substance can be given to the patient so that the blood pressure is raised. If the femoral head is avascular the pressure in it will remain unchanged. He estimates that this method will give an accurate diagnosis in 60% of cases.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Acroparaesthesia and the Carpal Tunnel

SIR,—Referring to your interesting leading article entitled "Acroparaesthesia and the Carpal Tunnel" (*Journal*, May 9, p. 1230), I can assure you that women between 40 and 60 years complaining of being awakened at night with painful paraesthesiae in the fingers and pain in the forearms, occasionally, but not often, as high as the shoulder, are not at all confined to neurological clinics. General physicians and surgeons, as, also, orthopaedic surgeons, frequently encounter these patients, and diagnosis is often difficult. Having at one time been assistant to the late Dr. A. W. Adson at the Mayo Clinic, who wrote so clearly on cervical rib, I have always been interested in the subject of pain in the upper limb, and feel that one of the great advances resulting from the recognition of the carpal tunnel syndrome on the one hand and cervical spondylosis on the other is that it has removed from the costo-clavicular space a number of suggested mechanisms said to be the cause of painful arm. Hypertrophy of scalenus anticus, bands in Sibson's fascia, nipping between clavicle and normal first rib, post-fixed plexus, have all been blamed, yet their correction by exercises strengthening the muscles elevating the shoulder-girdle, or by operation, fails to give relief, or gives it only temporarily.

My own view, resulting from over 80 cases, is that the paraesthesia or motor disturbances resulting from cervical rib or cervical band are precise in pattern, corresponding to the distribution of the first dorsal nerve. There may be a little overflow when pain is severe, but vague or widespread never. This is amply proved by operation for cervical rib or band, when this precise paraesthesia is abolished and the motor dysfunction is halted, though motor power is rarely restored; and one can promise this result with confidence. But if pain is described as affecting the arm and forearm, perhaps spreading up to the neck or side of chest, and almost always without muscle wasting, it is not due to anything in the costo-clavicular space, even though a cervical rib be present; and removal of the rib will fail to relieve the condition. Such widespread pain is much more likely to result from cervical spondylosis. When the pain or paraesthesiae are confined to the forearm and especially outer border of hand, pressure on the median nerve in the carpal tunnel is the likely cause. Unfortunately, cervical spondylosis is common and one meets with patients suffering at the same time from both spondylosis and the carpal tunnel syndrome; and soon a psychogenic factor becomes superimposed.

Not the last has been said about the carpal tunnel syndrome, for, quite apart from its relationship to old trauma and rheumatoid arthritis of the wrist-joint, it is not clear why in some cases one sees at operation the nerve just tightly accommodated in its fibro-osseous canal, whilst in others a pinkish nerve looking as if the tightness is because the nerve itself is swollen. Regarding the tendency for the pain to be worst in bed at night, I have always thought this to be due to the generalized peripheral vasodilatation that occurs during sleep, thus adding to the squeeze already present in the tunnel. Finally, I would like to repeat what I have thought for 10 years or more and which continued experience has confirmed—namely, that the vascular phenomena associated with cervical rib only occur when the arch of the subclavian artery is high.[1] This arch is variable, in some people only just palpable above the clavicle, in others reaching a good 5 cm. above the clavicle, and it is the latter arrangement that brings the junction of the second and third parts of the artery in contact with the extra rib, against which it is squeezed about 20,000 times a day by the scalenus anticus muscle. Gruber's (1869) grades 2 and 3 cervical ribs are the ones most likely to affect a highly arched artery in this way, and, after many years, thickening and thrombosis may result; rarely, aneurysm.—I am, etc.,

Department of Surgery, University of Birmingham. F. A. R. STAMMERS.

REFERENCE

[1] Stammers, F. A. R., *Lancet*, 1959, **1**, 603.

SIR,—It is open to question whether the acroparaesthesia of the middle-aged woman is due to a lesion of the median nerve. When this nerve is involved in, for example, arthritis of the wrist, the patient complains of numbness in the distribution of the nerve and weakness and wasting of the muscles supplied by it. The woman with acroparaesthesia complains that she cannot sleep because every night she is awakened by the well-known and distressing symptoms, and she may have to get out of bed and pace the room for an hour, or occupy herself making tea, before she can get back to rest: there is no loss of power and no loss of sensibility. Furthermore, if one is careful to avoid leading questions in taking a history one will find that the little finger is occasionally involved as much as any of the others.

It is of great interest that the injection of 0.5 to 1 ml. of hydrocortisone into the carpal tunnel provides dramatic relief in a high proportion of cases, including those occurring in pregnancy. This may be long lasting and may even obviate division of the retinaculum. Why should this be so? If one looks at the cross-section of the wrist it becomes clear that an injection will most likely find its way into the tendon sheaths, and therefore it seems to me reasonable to suggest that this variety of acroparaesthesia may be due to a lesion of the tendons themselves (or their sheath) rather than the median nerve.—I am, etc.,

Birmingham, 15. W. M. PHILIP.

SIR,—Your excellent leading article on this subject (*Journal*, May 9, p. 1230) presented an unkempt appearance because of the loose ends sticking out all round it. You enumerated the diagnostic points, you mentioned some aetiological theories, and you described two methods of treatment, but you did not explain why shoulder-girth exercises should relieve some cases, nor why pain, swelling, and paraesthesia should occur at night, and the explanation of the reproduction of symptoms with a sphygmomanometer cuff was somewhat bizarre.

The cause of the symptoms is pressure on the median nerve. The pressure on the median nerve is due (in the absence of demonstrable cause) to oedema of paratenon in the carpal tunnel. The question is what produces this oedema, especially in women between the fourth and sixth decades after heavy housework, and

why is it usually at its worst in the early hours of the morning. The timing of the attacks gives the clue. Paraesthesia of the hands occurring at night is usually due to the position of the neck in sleep. So large a proportion of these cases have a cervical spondylosis that one is tempted to say that, in those where cervical radiographs show no degenerative changes, these changes must be present in some periarticular tissues anterior and posterior to the intervertebral canals. Pull by the trapezius on cervical vertebrae, inevitable with heavy housework, irritates and swells up the nerve roots during the day; an inadequately supported neck dropping into flexion compresses them at night; pain in the arm is due to root pressure; oedema in fingers and paratenon must result from involvement of sympathetic pathways.

Grant this and the whole mystery resolves itself. That shoulder-girdle exercises should be beneficial is explained, and how venous occlusion by the sphygmomanometer cuff increases the oedema and reproduces symptoms is at once seen. It is no longer a matter for surprise that there is frequently pain higher up the arm. While division of the volar retinaculum relieves many, and a night splint, preventing wrist flexion, improves lymphatic drainage of the area, cervical manipulation also proves effective in a number of cases and deserves a trial in all of them.—I am, etc.,

London, W.1. JOHN EBBETTS.

SIR,—Your leading article on acroparaesthesia (*Journal*, May 9, p. 1230) stresses the well-known difficulty of distinguishing between pins and needles felt in the hand as the result of: (1) root-pressure in cervical spondylosis; (2) the thoracic outlet syndrome; (3) friction on the median nerve in the carpal tunnel. A number of differentiating criteria exist, however, based partly on applied anatomy but partly on an undescribed phenomenon. This is the different behaviour of pins and needles when caused by pressure on (*a*) a nerve root; (*b*) the proximal part of a nerve trunk. When a nerve root is compressed, the pins and needles constitute a *pressure* phenomenon, ceasing as soon as the contact ceases. In pressure on a nerve trunk, the pins and needles are a *release* phenomenon, appearing some time after pressure has been relieved.[1] The longer the pressure has lasted, the longer after release it takes the pins and needles to come on.

Differential diagnosis can be based on these phenomena.

Timing.—In spondylitis the pins and needles are usually continuous; in the thoracic outlet they are nocturnal; and in the carpal tunnel syndrome they are aggravated by use of the hand.

Distribution.—In spondylitis, the pins and needles occupy the distal extent of a dermatome and are felt inside the digits, not on any one aspect. In the thoracic outlet syndrome, usually all the digits of both hands feel paraesthetic, whereas friction on the median nerve gives rise to pins and needles felt only at the palmar aspect, omitting the little finger.

Provocation.—In spondylitis, some of the neck movements cause scapular aching, but seldom an increase in the digital paraesthesiae. In the thoracic outlet syndrome elevation of the scapulae or of both arms lifts the lower trunk of the brachial plexus off the first rib. Either posture, maintained for two to ten minutes, brings on pins and needles owing to release. In the carpal tunnel syndrome, moving the fingers with the wrist held in full extension sets up paraesthesiae.

Relief.—In spondylitis, traction on the neck stops the pins and needles for as long as the pull is maintained. In the thoracic outlet syndrome, the patient finds that sitting up or hanging the arm down over the edge of the bed re-establishes pressure on the nerve trunk and thus stops the pins and needles for the time being. In the carpal tunnel syndrome, splinting the wrist stops the friction and thus the pins and needles.

Since most patients with acroparaesthesia of whatever provenance are middle-aged, an *x*-ray photograph of the neck is very apt to show evidence of spondylitis whatever the actual condition may be. Hence clinical examination remains paramount, and if the criteria listed above are taken into account real difficulty is seldom experienced.—I am, etc.,

London, W.1. JAMES CYRIAX.

REFERENCE

[1] Cyriax, J., *Textbook of Orthopaedic Medicine*, 1957, 3rd edition. Cassells, London.

Midwives and Oxytocin

SIR,—Attention has recently been drawn to the apparent rule of the Central Midwives Board about the administration of "pitocin" (oxytocin). This is alleged to demand the "physical presence" of the practitioner ordering the drug throughout the whole period of its administration. If this is rigidly enforced it clearly precludes its use in the medical induction of labour both in the home and in any maternity unit where there is no resident doctor. This appears to me to be a retrograde step.

I have never seen any harmful effects from the exhibition of this drug in the usually recommended dosage in over 10 years of obstetrics in both hospital and general practice. I have discussed this matter with general-practitioner and consultant colleagues in active clinical work, and they appear in general agreement with my opinion.

It would be of interest to hear the views of the profession at large on: (1) The use of oxytocin. (2) The ability of the Central Midwives Board indirectly to impose restrictions on a medical practitioner.—I am, etc.,

Guildford. JOHN S. TAYLOR.

Diabetes in the Tropics

SIR,—I was interested to read Dr. W. B. Waddell's letter in your issue of April 25 (p. 1120) in further extension of the arguments developed in your leading article entitled "Diabetes in the Tropics" (*Journal*, January 24, p. 219).

For many years Buerger's disease was considered an illness limited to Jews, because it was first described in Jewish patients. The power of recovery from diabetes is now described from Africa and Asia, and repeat glucose-tolerance tests are reported normal several months after a course of treatment with insulin or tolbutamide. May I suggest that the variable in the cases reported was not their geographical or racial situation but the simple fact that a repeat glucose-tolerance test was in fact performed?

The writer's personal experience suggests that temporary diabetes, of varying degrees of severity, is a far from rare occurrence. If we physicians in the more balmy climates would begin to consider diabetes as not an invariably permanent condition, if we were to open our minds a little and remove our fixed gaze from insulin, the anti-diabetic panacea, wonderful though it is when we really need it, we would receive many

surprises. A slightly more critical attitude to treatment, and an attempt to reduce insulin or the sulphonylureas whenever possible, to withdraw them even, has for several years suggested to me the frequent temporary nature of the disease. It is suggested that in suitable diabetic centres attempts might be made to systematically organize patient material in such a way that six-monthly repeated glucose-tolerance tests might give us a real clue to the nature and time limitation of the diabetic state.—I am, etc.,

Johns Hopkins Hospital, Baltimore, U.S.A. FREDERICK WOLFF.

Oral Antidiabetic Agents

SIR,—Professor W. J. H. Butterfield and Dr. C. Hardwick will I hope forgive me if I challenge the view given in their letter (*Journal*, May 16, p. 1298) on the mode of action of the sulphonylureas, where they stated that "nothing found so far contraverts the suggestion that the oral antidiabetics stimulate the secretion of endogenous insulin." This statement was supported by references to the ingenious and painstaking experiments of Professor Butterfield and his associates on the glucose uptake of the forearm tissues in man. Further references (see letter) were made to the work of Williams *et al.* and Lundbaek *et al.*, which indicated a direct effect of these compounds on the uptake of glucose by muscle tissue.

However, other workers[1,2] (and these references were not cited) have failed to demonstrate any effect of these compounds on glucose uptake by the rat diaphragm technique. Further, using this same technique, no increase in the serum insulin levels has been observed following treatment with these drugs.[3,4] In addition neither the concept of a direct insulin-like effect nor of a stimulation of endogenous insulin secretion are supported by studies on the usual concomitants of an increased insulin effect such as changes in the respiratory quotient and nitrogen, lactic, and pyruvic acid metabolism.[5] In contradistinction there is evidence (also uncited) indicating an effect of the sulphonylureas on glucose release from the liver.[6,7] The current compromise in the B cytotrophic hypothesis is that insulin secreted endogenously into the portal circulation has a primary effect on hepatic glucose release rather than on the peripheral utilization of glucose. There is a certain amount of experimental support for this theory,[8,9] but even this is obviously not in agreement with the work cited by Butterfield and Hardwick which proposes a peripheral site of action.

All the clinical evidence certainly supports the view that these compounds work only in the type of diabetic patient who still has some endogenous insulin secretion, but it does not necessarily follow that an increase in this insulin secretion is involved in their hypoglycaemic effect. In terms of the classical argument about diabetes mellitus as a disease of under-utilization of glucose versus over-production of glucose, in which the blood glucose level is represented as fluid in a tank, then an effect on the level of the fluid is only clearly manifest when both the inflow and outflow from the tank is being controlled. Thus, should the sulphonylureas act mainly or entirely on the hepatic release of glucose, then this effect would be clinically appreciable only in those patients who still had adequate utilization of glucose (hence the dependence on some endogenous insulin secretion). Furthermore, from a teleological point of view I doubt whether "diseased" islet tissue is capable of increased stimulation for a prolonged period without exhaustion setting in (our own long-term studies show secondary failure to be a rare sequence).[10] In any case the islets are already under the best-known stimulus to increased insulin secretion—a raised blood glucose level.

Professor Butterfield and Dr. Hardwick have done a service in raising the problem of the mode of action of sulphonylureas in the correspondence columns of the *Journal*, since it is difficult to present adequately the more contentious aspects of this problem in an article. It is, however, unfortunate that they should add to the literature in support of the sulphonylureas as B cytotrophic agents without a discussion of the difficulties raised by some of the work cited above. For, even if some of this evidence does not contravert the suggestion that the oral antidiabetics stimulate the secretion of endogenous insulin, it certainly makes its acceptance or understanding more difficult. At present we do not know how these drugs act any more than we know how insulin acts, and it is significant that it has taken 37 years to define our ignorance in this field.—I am, etc.,

Metabolic Department, Royal Victoria Hospital, Belfast. J. A. WEAVER.

REFERENCES

1 Field, J. B., and Woodson, M. L., *Proc. Soc. exp. Biol.*, (*N.Y.*), 1956, **93**, 534.
2 Cahill, G. F., jun., Hastings, A. B., and Ashmore, J., *Diabetes*, 1957, **6**, 26.
3 Weaver, J. A., Prout, T. E., Scott, G. W., and Asper, S. P., jun., *Brit. med. J.*, 1958, **1**, 425.
4 Seltzer, H. S., and Smith, W. L., *Proc. Soc. exp. Biol.* (*N.Y.*), 1959, **100**, 171.
5 Editorial; Stadie, W. C., *Diabetes*, 1958, **7**, 61.
6 Vaughan, M., *Science*, 1956, **123**, 885.
7 Ashmore, J., Cahill, G. F., jun., Earle, A. S., and Zottu, S., *Diabetes*, 1958, **7**, 1.
8 Madison, L. L., and Unger, R. H., *J. clin. Invest.*, 1958, **37**, 631.
9 Jacobs, G., Reichard, G., Goodman, E. H., Friedmann, B., and Weinhouse, S., *Diabetes*, 1958, **7**, 358.
10 Gorman, C. K., and Weaver, J. A., *Brit. med. J.* (in press).

Community Care of Mentally Ill

SIR,—Concerning the Report of the Royal Commission on the Law Relating to Mental Health, in a memorandum which has been issued by executive councils to general practitioners (E.C.N. 297) appears something which cannot but cause anxiety and suffering to many in our community.

"The Report suggests that the division of functions between the local authorities, the hospitals and other official bodies should be broadly the same in relation to mental disorders as in relation to other types of illness or disability. This implies a considerable expansion in the services provided by local health and welfare authorities for the benefit of the mentally disordered. It means too an increase in the numbers of mentally disordered persons who will remain in the community, if possible in their own home surroundings, and who will be cared for there."

In what way this cold, rather sinister official statement affects me I may best convey by relating from my personal experience one case.

When I was young and anxious for power to cast out devils I found myself in charge of mentally afflicted patients. The atmosphere of hopelessness which blanketed this branch of medicine gradually chilled my ardour. One day a young man was admitted, roughly speaking, kindly and harmless but troublesome. He soon settled down to the routine of institutional life, and later I had an interview with his nearest relative, a mature man holding very considerable national responsibility. His words altered my warped viewpoint, and I was given a glimpse of the community outside the encircling walls. "I cannot thank you too much for looking after my stepbrother. My two sisters have devoted their lives to his welfare. They were becoming prematurely old. Now they are living."—I am, etc.,

Haydon Bridge, Northumberland. RICHARD BELL.

Student Suicides

SIR,—Since Sir Alan Rook presented his valuable study of student suicides (*Journal*, March 7, p. 599), correspondents have continued his discussion of the aetiology of these and other psychiatric breakdown among students, and of the steps which can be taken by the student health services to prevent them, or to treat them in their early stages.

But preventive measures should begin much earlier. The great majority of these students have vulnerable personalities and succumb to stresses which others surmount unscathed. The seeds of their breakdown have been sown long before. In interviews with such patients it is usually found that a demonstrable degree of maladjustment has been present for many years. There is a special opportunity for valuable preventive work in the pre-university years, when the intelligent adolescent is commonly in an introspective phase, preoccupied with himself and with the problems of growing up, ready to talk and not unreceptive in his attitude towards professional help, once he is convinced that the psychiatrist has something to offer.

Opportunity comes in the first instance to the family doctor and to the school medical officer. It is for them to recognize that an intelligent adolescent who, for example, loses his or her capacity to work and does not know what to do, rows endlessly with the family or develops psychosomatic symptoms, may be showing manifestations of potentially serious illness which should be investigated, not dismissed as tiresome "teen-age" behaviour. These young people are often profoundly unhappy. It is for the general practitioner or school medical officer to persuade the patient, the parents, and sometimes the headmaster that something can and should be done to help them. Opportunity comes in the second place to our psychiatric clinics. There is a special responsibility on them to provide adequate services for these gifted adolescents and to present them in an acceptable form.—I am, etc.,

The Tavistock Clinic, London, W.1. DUGMORE HUNTER.

Intermittent Suxamethonium Injections

SIR,—I have read with some consternation in the *Journal* of March 21 (p. 786) the letter by Dr. J. Bullough on the alleged dangers arising from the intermittent administration of succinylcholine chloride.

I am convinced that anaesthetists who have been using this relaxant for years—whether as a single dose, intermittently, or as a continuous drip—will not agree that it should be held responsible, *per se*, for the phenomena imputed by your correspondent. Bradycardia, cardiac arrhythmia, and hypertension occurring during general anaesthesia were known long before the advent of the muscle relaxants. They are now recognized as conditions arising from the ill effects of hypoventilation[1]—namely, hypoxia and hypercapnia. It is also known that bradycardia and hypertension can occur when there is a build-up of intra-alveolar tension resulting from incorrect pumping of the re-breathing bag. Furthermore, there is no scientific proof whatsoever that succinylcholine has any deleterious effect on the cardiovascular system.

In the anaesthetic death reported, the doses of the inhalation narcotics recorded were: approximately 0.7% trichlorethylene, and 75% nitrous oxide with 25% oxygen. I find this statement not only of little value but misleading. Surely it is the amount which the patient *absorbs* which counts? And this depends mainly on the degree of respiratory ventilation—the *tidal volume*. Yet this all-important factor of respiration is not even mentioned by your correspondent, who merely states that at one stage the patient breathed by herself. One is left to assume that inadequate gaseous interchange took place, and therefore the possibility of hypoxia must be considered, although the anaesthetic machine might have been registering 25% oxygen. Again, with inadequate ventilation, one must assume also that insufficient carbon dioxide was excreted. In the absence of post-mortem data, the fatality appears therefore to be the sequel of hypoventilation, plus, more than likely, the poisonous effects of trichlorethylene which, having been absorbed but not excreted, exerted accentuated toxicity. The patient, who apparently was not a good risk, was unable to compensate adequately. There seems to be no valid evidence to indict succinylcholine as the scapegoat; nor is there any necessity to seek for an antidote in atropine. Groundless postulations, such as "the heart becomes sensitized," appear to be used far too glibly in general anaesthesia to cover a multitude of sins and can only bring the specialty into disrepute as a science. May I remind your correspondent that practically every weird, untoward, and so-called inexplicable phenomenon associated with general anaesthesia can be attributed to the concomitant state of hypoventilation which the anaesthetist has inadvertently allowed to occur?

It would appear more than possible that the 214 cases referred to by your correspondent are all examples of side-effects of hypoventilation occurring during the anaesthesias. I refer Dr. Bullough, and others who think along similar lines, to *The Man Behind the Bag*, by Lester Rumble, Jr.[2]—I am, etc.,

Johannesburg, South Africa. H. H. SAMSON.

REFERENCES

[1] Samson, H. H., *S. Afr. med. J.*, 1956, **30**, 470.
[2] Rumble, Lester, *Sth. med. J. (Bgham, Ala.)*, 1956, **49**, 368.

SIR,—In the correspondence on this subject I have not as yet seen a plain statement of the fact, which is surely well recognized, that suxamethonium exerts a muscarine-like action during its phase of depolarization. This is not surprising, for there is no reason why stimulation should be confined to the motor end-plates alone. The unwanted effects commonly noted by the anaesthetist are bradycardia and salivation, and both are abolished or reduced by atropine. It seems likely that all muscle relaxants of the depolarizing type would have a similar effect, but my own experience is mainly confined to suxamethonium.

The marked effect of a second dose alone, reported by Dr. J. Bullough (*Journal*, March 21, p. 786), is rather a different matter, and would require another explanation which I can make no attempt to give. My own experience suggests that any single dose of suxamethonium may produce marked bradycardia or transient vagal arrest in a susceptible patient.—I am, etc.,

London, S.W.5. T. A. BOLISTON.

SIR,—I have been much interested in the letters by Dr. J. Bullough (*Journal*, March 21, p. 786) and Drs. I. Verner and Christina Comty (*Journal*, May 9, p. 1239) on this subject; since both letters mention animal experiments, it may interest your readers to know that the Universities Federation for Animal Welfare (UFAW) is at present sponsoring a research programme on the effects of relaxants on animals, hoping thereby to gain information as to the most humane ways of using these drugs in veterinary medicine.

I have used suxamethonium bromide ("brevidil E") extensively in the rabbit as (1) single intravenous injection,

(2) repeated intravenous injections, and (3) intravenous drip; the relaxant has been used with and without pentobarbitone sodium ("nembutal") anaesthesia, and with and without atropine premedication. When atropine was used it was given as an intramuscular injection half to one hour before induction of anaesthesia, at a dosage of 2 mg./kg. body weight.

In my experience, if sufficient suxamethonium bromide is given to have any effect on the musculature (it produces spastic rather than flaccid paralysis), it causes bradycardia which is usually fatal under all the various conditions listed above. The dose/response curve for the rabbit is very steep, 0.11 mg. active cation/kg. body weight/min. (intravenous drip) having almost no effect on the musculature, and 0.12 mg./kg./min. producing fatal bradycardia.

The bradycardia is rapid in onset, occurring about 10 seconds after intravenous injection, or about 5 minutes after the start of an intravenous drip. Artificial respiration has no beneficial effect. Atropine does not prevent the trouble, though it may delay it. It is usually accompanied by extreme meiosis and often by marked peristalsis. Continuous recording of E.C.G.s shows that it is a sinus arrhythmia initially, though other irregularities occur in the later stages; electrocorticograms show that there is no irregularity in the activity of the cortex other than that due to failure of circulation.

Suxamethonium bromide is used fairly widely in veterinary surgery in the dog, and no similar trouble from bradycardia has been reported. I suggest that the rabbit is probably one of the most sensitive species for demonstration of this effect, though in my experience it is difficult to resuscitate a rabbit once bradycardia has occurred. I should be very interested to hear from any other readers who have had similar experiences in clinical or experimental work, since the pharmacology involved does not at present seem clear.—I am, etc.,

The Universities Federation for Animal Welfare,
7a, Lamb's Conduit Passage, London, W.C.1. PHYLLIS G. CROFT.

Treatment of Organophosphorus Poisoning

SIR,—There is now convincing clinical evidence for the value of pyridine-2-aldoxime methiodide (PAM) in the treatment of poisoning by the organophosphorus insecticide parathion, and experimental evidence of the value of PAM and other oximes in poisoning of animals by other anticholinesterase insecticides,[1] especially in combination with atropine therapy.

Both the methiodide (PAM) and the more soluble methane sulphonate (P2S) are available in this country as laboratory chemicals, but inquiries in late 1958 showed that no ready-to-use pharmaceutical preparation existed in North America or this country. Supplies of PAM have therefore been obtained from Japan in ampoules ready for immediate use. This preparation has been extensively and successfully used in that country for the treatment of parathion poisoning. Supplies of PAM have been located at the following establishments of this company, all of which are situated in areas of considerable insecticide usage:

Harston, Cambridge (Harston 312) (Day and night)	Staplehurst, Kent (Headcorn 213)
Feering, Essex (Kelvedon 257)	Fakenham, Norfolk (Fakenham 2313)
Metheringham, Lincs (Metheringham 206)	Lichfield, Staffs (Lichfield 3228)

These supplies are available on request to any practitioner encountering a case of organophosphorus poisoning. It should also be noted that the Medical Division, C.D.E.E. (Ministry of Supply), Porton, Wilts (Tel. Idmiston 211), also operates an emergency service for the treatment of any cases of organophosphorus insecticide poisoning.[2]

The recommended specific therapy of such cases is a combination of atropine, PAM (or P2S), and supportive measures.

Initially, atropine sulphate should be given (intravenously or intramuscularly), in doses of 2 mg. (1/30 gr.), to be repeated every 30–60 minutes until the patient is obviously fully atropinized or is improving. PAM should be administered intravenously as soon as possible, in doses of 1 g. (i.e., two 20-ml. ampoules each containing 0.5 g.). This dose of PAM may be doubled in very severe cases, or repeated after 30 minutes if no real improvement has occurred. A rather dramatic improvement is likely in all severe and responsive cases after the first injection. A "maintenance dose" of PAM may be given intramuscularly or subcutaneously where signs of poisoning tend to persist. Supportive measures may need to include intravenous or intramuscular barbiturates for intense excitement or restlessness, postural drainage for bronchial hypersecretion, and oxygen therapy for respiratory distress. In known or suspected swallowing of the poison, the stomach contents should be washed out as soon as possible. All cases should be kept imperatively at rest, as excitement and exertion may cause very marked increase in symptom-severity.

Since PAM actually reverses the cholinesterase inhibition caused by most organophosphorus insecticides, there is a possibility that the atropine dosage previously given may then become excessive and cause toxic effects—e.g., mental confusion. This may lead the physician to wrongly believe that the PAM therapy has been ineffective. PAM is only likely to be ineffective in poisoning due to certain O.P. insecticides (i.e., schradan, dimefox, rogor), but there is no evidence that it is contra-indicated in such cases. The chemical nature or name of the particular compound concerned can almost always be found on the label of the container.

Information of considerable future value in research could be obtained from cholinesterase determinations on successive blood samples from patients before and during oxime therapy.—I am, etc.,

Medical Department,
Chesterford Park Research Station,
Fisons Pest Control Ltd.,
Saffron Walden, Essex. E. F. EDSON.

REFERENCES

[1] Davies, D. R., and Green, A. L., *Brit. J. industr. Med.*, 1959, **16**, 128.
[2] *Lancet*, 1959, **1**, 981.

Breast Abscess

SIR,—In your annotation entitled "Breast Abscess" (*Journal*, May 16, p. 1288), a phrase is used which should not pass without comment: "whether hospital staffs, *perhaps largely for their own convenience*, too often insist on a mother breast-feeding while in hospital . . ." (my italics). If the convenience of the nursing staff were to be taken into account, far more babies would be bottle-fed. There is no comparison between the time and trouble of preparing artificial feeds and that involved in staying with a mother and baby and helping with the delicate mutual adjustments that go to the establishment of breast-feeding.

Only a firm belief that breast-feeding is in fact best for both mother and child could induce nurses to persevere in such an exacting task, though the occasional mother who, initially unwilling, finds unexpected fulfilment in feeding her own baby repays all their efforts.—I am, etc.,

Belfast. MURIEL J. L. FRAZER.

Psychotic Reaction to Atropine Drops

SIR,—Reactions such as have been described by Dr. P. J. Daly (*Journal*, April 18, p. 1043) are indeed rare, but they would be more rare still if it were realized that one drop of 1% atropine sulphate produces total cycloplegia in two hours.

I arrived at this conclusion many years ago after refracting a series of 50 children. The refraction was carried out at half-hourly intervals up to the end of two hours, after the instillation of one drop of atropine. Thereafter atropine was given daily for a week, and the refraction carried out once again. In no case was there found any further cycloplegia at the end of the week than was found at the end of two hours.—I am, etc.,

Southport General Infirmary. DAVID RANKINE.

Lumbar Puncture

SIR,—One of the most frequently noted drawbacks to spinal anaesthesia and also to lumbar puncture for other purposes is headache, said to be due to leakage of cerebrospinal fluid through the hole in the meninges. The needle commonly used for lumbar puncture is a wide-bore affair; for some reason I have never understood, the "Vienna" (or "Duttner") needle is apparently almost unknown in this country.

Whilst I was engaged in gynaecological surgery in India some years ago I rarely had the services of a trained anaesthetist, nor had the science of general anaesthetics reached its present remarkable efficiency. In consequence I almost invariably operated under spinal anaesthesia—with "nupercaine" (cinchocaine)—giving the anaesthetic myself through the Duttner needle, the use of which I had learnt in Vienna in 1930. It consists of a stout needle used to penetrate only through the intervertebral ligament, whilst a fine-bore needle inside it can then be pushed a further 1 cm. through the meninges to tap the C.S.F. From an experience in India of many hundreds of cases I found that under this procedure "spinal" headaches were practically unknown.—I am, etc.,

East Grinstead, Sussex. W. C. SPACKMAN.

Psychosomatic Disorders in Children

SIR,—I have read Dr. Lindsey W. Batten's article on psychosomatic disorders in children (*Journal*, April 25, p. 1109). Among the many points he raises in the study of the family environment he does not mention the helpful effect of exercise. This activity, with, it is hoped, fresh air, has always been a medical treatment. Sensible exercise can bring the necessary calm to the patient and peace to the skin or bronchioles. A similar peace is felt after the pain of the dentist or some specialist clearing "septic foci," and in some way must cause "new circuits" to be used or cleared.—I am, etc.,

St. Luke's Hospital, Armagh. D. G. MAYNE.

Hazards of Ship Surgeons

SIR,—In your issue of April 18 (p. 1051) your legal correspondent reviewed the medico-legal hazards of a ship surgeon and concluded his article with the timely advice that a ship surgeon should "ensure that his medical defence society covers him outside England."

Through its overseas indemnity scheme the Medical Protection Society has for over twenty years provided world-wide cover for members practising overseas with the exception of claims falling within the jurisdiction of the courts of the United States of America. The Society has recently recognized, however, that a member acting in the capacity of a ship surgeon is liable to be sued in the U.S.A. courts by a patient treated on board ship, and has decided to cover these members against this risk without any increase in the existing scale of subscriptions for overseas indemnity.—I am, etc.,

London, W.C.2. ALISTAIR FRENCH, Secretary, Medical Protection Society.

Subject in Search of a Name

SIR,—With reference to Professor L. J. Witts's letter (*Journal*, May 2, p. 1190) there is prejudice, which I share with Gordon,[1] against the use of the word "health" on the ground that attempts have been made to divorce it from medicine, with the mistaken idea that it is a nobler appellation, whereas the dividing line between one and the other is far from clear. On the other hand, we have the association of paediatrics with child health, which seems to pass without any degree of criticism, so it would seem that preventive medicine and public health could quite as easily go together.

Social medicine in its present usage refers essentially to the epidemiological method, including its application to the study of genetic as well as environmental and domestic factors in the aetiology of disease. Public health, alone, though not easily defined, does not seem to take into account this new aspect of comprehensive epidemiology. Environmental medicine or community medicine fails to include the vast field of knowledge, law, and practice which has accumulated under the term public health since the first Public Health Act of 1848. Like many other terms, the connotation of hygiene has altered over the years, yet the *Concise Oxford Dictionary* defines it as "Principles of health; sanitary science." The bias at the present time would appear to be towards the second meaning, so that alone it could not stand for this "subject in search of a name," but, coupled with preventive medicine and given its full meaning, this branch of medical knowledge could be called "Preventive Medicine and Hygiene."—I am, etc.,

Birmingham, 13. V. A. LLOYD.

REFERENCE

[1] Gordon, I., *Lancet*, 1958, **2**, 638.

SIR,—Professor L. J. Witts's invitation (*Journal*, May 2, p. 1190) for a name for the subject variously known as public health, epidemiology, social medicine, human ecology, population pathology, or group medicine makes me wonder whether the term "Mass Medicine" would not fit the bill, as this adjective is already used in "Mass Miniature Radiography," where also a collection of people are studied.—I am, etc.,

Wilmington, near Dartford, Kent. RUDOLPH PAYNE.

SIR,—If my memory does not fail me, public health has been called "environmental medicine." Even though it sounds nice, it has not gained much popularity. Perhaps we can include public health, social welfare, etc. (*Journal*, May 2, p. 1190), under the term "external medicine."—I am, etc.,

East Fortune Hospital, North Berwick. M. S. N. RAO.

Plastic Bags

SIR,—A few months ago a little girl patient of mine was found lying unconscious on the pavement with a "cellophane" bag over her head held in place round the neck by a rubber band. Fortunately, this was quickly removed, and after a short period of unconsciousness she recovered.

I note in *The Times* of May 19 a report that twenty children have died in the U.S.A. over the past year from asphyxiation by using a transparent plastic bag as a space helmet, etc., and that a law has been proposed there to compel the makers of these bags to print a warning notice on them. Since this sort of accident may be more common than is realized and may become more common still with the increasing use of these bags, I feel justified in reporting this incident.—I am, etc.,

Amble, Northumberland. R. P. ROBERTSON.

POINTS FROM LETTERS

Thank the First-aider

Mr. FREDK. C. REEVE (Hove, Sussex), formerly technical editor of *First Aid and Nursing*, writes: May I appeal, through your columns, to all surgeons, but especially to casualty officers? Only those who have been associated with the voluntary ambulance movement for many years know the enormous value of a few words of praise and congratulation offered by the surgeon to the first-aider who has correctly treated a casualty brought to him. . . I would ask all surgeons, therefore, not to omit those few words of praise when deserved.

Personal Medical Record Disks

Dr. L. I. NORMAN (Blackheath) writes: Dr. K. Southgate's letter (*Journal*, April 25, p. 1122) on medical records is certainly interesting. It is based on the assumption that all doctors keep notes, and further that these are legible. I do not think the facts are so. Most doctors who keep notes usually do so for their own benefit, and not for those who follow after. I base this assumption on the medical records that follow new patients to this practice.

Radiation and Leukaemia

Dr. PAUL HAMMET (Bilston, Staffs) writes: May I voice my dismay at the apparent lack of concern evinced by the authorities over the rate of increase of ionizing radiation, specifically the doubling of osteophilic strontium-90, particularly since it is becoming increasingly doubtful that there is such a phenomenon as a "safe limit"—i.e., a critical aplasiogenic or sarcogenic dosage or dose rate? Certainly the results of studies recently published (see *Journal*, April 25, p. 1095) show how unwise it is to be unduly complacent in view of the statistical increment in the incidence of deaths from acute and myeloid leukaemia, which can hardly all be due to increased use of radiological apparatus. . . . Our vocation is to preserve health and life. Is it not clearly our inescapable duty to protest in unison and with emphasis against the nuclear psychosis afflicting our world? Or do we prefer to wait until we are poisoned in our surgeries, or even blasted with radioactive fire on the golfing green?

Too Many Tonsillectomies?

Dr. C. MEKSUPA (Bangkok) writes: I have read with interest the letter by Mr. J. McFarland (*Journal*, February 21, p. 509). Being a general practitioner, I am doubtful about his statement concerning the use of antibiotics in tonsillitis. If it is agreed that tonsillectomy should be the last resort, then I think antibiotics are strongly indicated whenever there is an acute attack. In my experience the unlimited use of antibiotics is the only means of avoiding the operation, especially in the young and early cases.

Obituary

G. C. RAMSAY, C.I.E., O.B.E., M.D., D.T.M.&H.

Dr. G. C. Ramsay died in Ayr on May 15. More than anyone else he had shaped the attitudes towards the methods and possibilities of controlling malaria in India in the days before D.D.T. made it relatively easy, bringing a fine brain and much industry to solve a problem of great importance. His original studies of epidemiology and entomology led to the formulation of principles of control which were entirely new in India, and which for the first time made it possible to control transmission of the intense malaria which occurs in Assam and parts of Bengal.

Born in Dunfermline in 1889, Graham Colville Ramsay was educated at George Heriot's School and Edinburgh University, where he was a medallist in the M.B., Ch.B. finals in 1912 (he later graduated M.D. with commendation). After house appointments he went to Cachar in the Surma Valley of Assam as assistant to Dr. H. J. Glover, who was medical officer to a major group of tea companies in this remote and particularly unhealthy place. This practice was already exceptionally progressive, and with this record of past achievement and the later management of Dr. Ramsay and his successor, Dr. G. Fraser, it was destined to become unique amongst tea practices by its combination of stability, elaboration of services, standards, and contributions to knowledge.

Ramsay's connexion with India was temporarily broken by the first world war, for he served from 1914 to 1919 in the R.A.M.C. He was first sent to France, but later moved to Mesopotamia, the Hedjaz, and Syria, where he served in personal contact with T. E. Lawrence and became medical officer to King Feisal and to the Arab Medical Administration in Damascus. After the war, in 1919, he married Muriel Fulham and returned to Cachar as principal of the practice, where he developed a passionate interest in the control of the malaria which dominated the health picture of all the inhabitants of the estates for which he was responsible.

The disease was ubiquitous, and no practical measures of control other than continued administration of quinine were available. He undertook a series of epidemiological and entomological studies which resulted in a much more precise definition of the nature of happenings in this intensely malarious area than had previously been possible. He incriminated *Anopheles minimus*, which he showed to be almost the sole vector. He analysed the breeding habits of this carrier and all the other anopheline mosquitoes in his area, and at the same time studied the incidence of malaria in relation to local topography. These studies were hailed at the time as brilliant and fully proved their value in subsequent experience. They made it possible to develop the principle of species sanitation which had been enunciated and practised in Malaya by Malcolm Watson but which had never been extended to India. Ramsay was thus able to show the exact circumstances in which malaria occurred, how it could be avoided, exactly what insect carried it, exactly in what circumstances the insect bred, and how the terrain could be modified to prevent it breeding. His work produced a new era of hope in the control of malaria which was of great importance to the people and the tea

industry of Assam and Northern Bengal. He became closely associated with Ronald Ross and with Malcolm Watson, both of whom visited him and at whose request he formed the India Branch of the Ross Institute, becoming the first principal in August, 1930. In that position he worked continuously to see the application of the methods which he had developed. While he was unable to continue personal research, he gave great encouragement to its practice by other doctors in similar situations to the one he had occupied, and there thus developed a series of laboratories in different parts of India for which he arranged financial subsidy and to which he gave personal advice and help which led to much further clarification of the malaria situation. It was in one of these laboratories in Southern India that the transmission of malaria in the southern hills was analysed: much of value came from one at Juri in Sylhet, and many contributions continued to come from his old laboratory in Cachar, which remained his great interest.

He was an active participator in medical affairs, president of the Assam Branch of the British Medical Association in 1925–6, chairman of the Surma Valley Division for several years, and a great contributor to the scientific discussions of the Branch at its annual meetings. By the application of his principles, malaria in Assam became for the first time controllable, and the pattern of life in a great part of the country was thereby materially altered. He was the esteemed principal of the India Branch of the Ross Institute, which prospered well under his able administration. He was the tutor and friend of a whole generation of medical practitioners and planters in Assam, as well as a serious contributor to scientific literature, especially on the epidemiology and control of malaria.

He had many distinctions throughout his life, starting with academic honours won in various examinations. His service in the first war led to a mention in dispatches and the appointment to the O.B.E. and to the Syrian Order of El Nahda. In 1931 he received the Kaisar-i-Hind Gold Medal in recognition of his researches on malaria, and in 1937 he was gazetted C.I.E. in recognition of the practical use he had made of those researches. He retired in 1946, and later lived for some time in South Africa, though his last illness occurred in Ayr. He leaves a widow and two daughters, to whom the sympathy of his very many friends will be extended.—G. M.

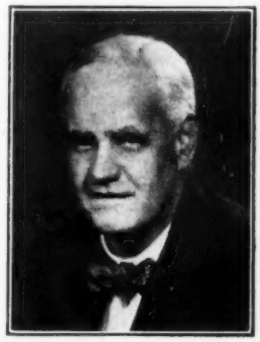
G. F. writes: Graham Ramsay was a most cheerful and engaging personality with a youthful, puckish expression, an ever-twinkling eye, a great sense of humour, and a tremendous zest and energy. With it all he was determined and forceful in his convictions, especially those relating to his professional life work, the control of malaria. In these he was a truly fervent missionary, and even his social talents were ultimately directed to win disciples to this cause. As he trudged around Assam tea gardens in the monsoon (he was a great believer in monsoon touring) putting up in different planters' bungalows every other night, he became a warm friend and welcome visitor, and sooner or later Ramsay convinced his hosts by his earnestness of the rightness of his views, and persuaded them to give his methods a trial. Generally he succeeded, by the results and by his own tireless enthusiasm and strenuous example, not only in winning their eager co-operation in routine control measures but in providing the facilities for and assisting in new experiments—in which draining, damming, shading, sluice gates, and siphons might all play their part—without which the work of Ramsay and his band of colleagues, the estate medical officers, would have made little headway. In the same way he generated tremendous enthusiasm among his fellow doctors, the estate medical officers, by his dynamic personality, welding all into willing teams which became the real field units of the Ross Institute in India. He, on his part, repaid them in whatever way he could, returning help for help and loyalty for loyalty wherever and whenever it lay in his power.

As well as being a friend and adviser he also maintained an excellent liaison in many ways and at all levels between employers in India and at home and the planters and doctors of the estates. He had his reward in the fruits of his work over a vast field, and the esteem and affection of his friends and colleagues.

F. R. EDDISON, M.R.C.S., L.R.C.P.

With the death of Dr. F. R. Eddison on April 13 Bedale and district lost a most valued member of the community.

Born more than 85 years ago, Francis Ryalls Eddison was a member of a well-known Leeds family, his father being an agricultural engineer and his uncle physician to the Leeds General Infirmary. He was educated at Bedford School and St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1898. After holding the appointments of house-surgeon at Addenbrooke's Hospital, Cambridge, and resident medical officer at the Royal Free Hospital, he came to Bedale, Yorkshire, in 1902 to join the late Dr. Tom Horsfall. He remained in that practice until 1958—56 years, broken only by war service. In 1914 he received a commission in the R.A.M.C. and saw service on the Salonika front, being twice mentioned in dispatches. He was demobilized with the rank of colonel.



In 1902 no one could foresee what the arrival and settlement in Bedale of that young man of 29 was to mean to the district during the next 57 years. He was the ideal family doctor, and every year he became more firmly established in the hearts of those among whom he lived. No patient could fail to remember his happy smile and cheerful greeting when he entered the sick-room, and seated at the bedside he would inspire the invalid with the greatest confidence by his unhurried and careful examination and reassuring attitude, rich and poor receiving the same courtesy and consideration. In his earlier years, when hospital amenities and ambulances were not available and journeys had to be made on horseback, emergency operations had to be performed in private houses: these operations Eddison would conduct with confidence and skill. He held numerous appointments, including those of local medical officer of health and honorary surgeon to the Rutson Hospital, Northallerton, but the appointment which appealed to him most was the office of H.M. Coroner for the Western District of the North Riding of Yorkshire. This work extended over a very wide area, reaching as far as the boundaries of Westmorland and Durham, and throughout this area he had a reputation for kindliness to those in trouble and for his shrewd judgment in guiding juries to a fair verdict.

He gave a great deal of his time to public work, serving on the North Riding insurance and local medical committees. Always ready to help in any social events, he was often called upon to address gatherings and societies on literary and other subjects. During the last few years he suffered from a crippling illness, which he endured with characteristic cheerfulness and fortitude.

He leaves a widow, three daughters, and one son, to all of whom the sympathy of the whole district goes out in the great loss they have sustained.

A neighbouring colleague writes: A pair of broad shoulders, a tall powerfully built frame, and a visage which breathed friendliness and good humour, a voice pleasantly modulated with well-chosen words and sentences even in ordinary conversation—all combined to win the hearts of

those who met this courteous member of our profession on his unhurried path through life. Nothing ruffled him, nothing dismayed him, nothing daunted him. His life as a country doctor began when the country doctor could only with great difficulty obtain specialist help, when there were few aids to diagnosis, when surgical emergencies had to be dealt with on the kitchen table by the man on the spot.

Francis Eddison always inspired confidence, not only in his patients but in those who were privileged to work with him, and by his exceptional hospital training he was quite capable of dealing with acute appendix, strangulated hernia, or perforation. All fractures were tackled as a matter of course. He used to say that one had to live with one's failures as well as with one's successes, and infinite care and considerable skill resulted in few of the former.

His good humour made him a delightful companion in his car or by his fireside, and a fund of anecdotes enlivened his conversation and his public speaking, of which he was no mean exponent. He was, perhaps, seen at best in his coroner's court. His dignified serious bearing, his shrewd and immediate grasp of a situation, his kindly treatment of witnesses, especially the bereaved, made him an outstanding coroner for almost thirty years. Osteoarthritis of hips rendered him at first relatively and then completely immobile, but he carried on with a measure of his work with great courage and without a vestige of self-pity—a fitting close to a long life of toil—displaying to the end the qualities which endeared him to his many friends and a host of patients.

ARTHUR HARRIS, M.D., D.P.M.

Dr. Arthur Harris, physician to the Bethlem Royal Hospital and the Maudsley Hospital, died in London on May 22. He was 50 years of age.

Arthur Harris was born on July 18, 1908. He already had a degree in economics when he took up the study of medicine at Manchester, his native city. After graduating M.B., Ch.B. in 1934 he became a house-physician at the Liverpool Stanley Hospital and in 1936 he joined the L.C.C. mental hospital service. It was at this period of his life that he proceeded to the M.D. in 1938 with a thesis on the treatment of schizophrenia, and in the previous year he obtained the D.P.M. of the English Royal Colleges. After service at Bexley, Hanwell, the Maudsley Hospital, and the St. Francis observation ward he joined the R.A.F. in 1942 and became a specialist in neuropsychiatry with the rank of squadron leader.

At the end of the second world war he returned to the Maudsley and was acting medical superintendent in the transition period before the inception of the National Health Service. In the many changes that occurred in July, 1948, the Maudsley Hospital and Bethlem Royal Hospital were combined as the postgraduate teaching hospital in psychiatry. Medical became replaced by lay administration, and Harris was elected chairman of the medical committee, a post of special importance at that time. He gave valued service in this position and as a member of the board of governors of the hospital. He was also a member of the academic board of the associated Institute of Psychiatry, and was a recognized teacher of the University of London. For several years he served on the Psychological Medicine Group Committee of the B.M.A. and on the Joint Committee of the Group Committee and the Royal Medico-Psychological Association.

D. L. D. writes: In the early days of the National Health Service many problems of medical reorganization had to be faced, and it was in large measure due to the personal influence of Arthur Harris that these were solved at the Maudsley with the minimum of friction and a workable machinery evolved which has met all subsequent requirements. He brought to bear on these problems a great fund of common sense, patience, and a capacity to distinguish what was really important. He never sought personal gain and was utterly devoted to the hospital which he served. On matters of medical planning and policy, memoranda would be required for guidance, and it nearly always fell to Arthur Harris to prepare these. After the passage of years the wisdom which he injected into such drafts is evident even more clearly than at the time of preparation.

His clinical interests, characteristically, were in the severely ill and the chronic sick. His early work was on the "cardiazol" treatment of schizophrenia, and among his latest was a critical investigation into the value of insulin treatment for that condition. Realizing the limitations of current therapies in such a disabling illness, he turned his attention increasingly to the social problems involved and published many papers dealing with rehabilitation. He was one of the pioneers of the psychiatric day hospital. Because of his drive and interest an old house next to the Maudsley was converted for this purpose, and when a cricket pavilion at Bethlem reverted to hospital ownership he seized the opportunity to show how cheaply and expertly it could be adapted to the same end. Later he grafted a night hostel on to his day hospital to serve still further the socially handicapped. Few patients were too far gone for some kind of help in his scheme of assessment. With the general decline of deep insulin therapy empty beds began to appear in the ward set aside for this purpose, and he used this opportunity to collect some of the prognostically hopeless who came to the hospital, many of whom achieved a surprising degree of social improvement under his care.

To his registrars he was a somewhat avuncular figure, ready with advice and encouragement to take up clinical investigations. His hobby was motoring abroad, and no sooner had he returned from one such trip than he began to make plans for his next. He would study the country he proposed to visit, its history, climate, food, and wines. He was an excellent host and liked to entertain visitors from countries he had visited or intended to visit. He made two Continental trips after his first heart attack in 1956 and seemed to be fully recovered when he was again struck down.

Our sympathy goes out to his widow, who was his perfect companion and shared his interests to the full. He will be sorely missed and always remembered.

W. K. PARBURY, M.R.C.S., L.R.C.P., D.P.H. D.M.R.E.

Dr. W. K. Parbury, formerly radiologist to the Bedford County Hospital and the Kettering and District General Hospital, died at Bedford on May 8. He was 93 years of age.

H. P. B. writes: Walter Key Parbury was a remarkable man who led a varied and remarkable life. Nearly 6 ft. 6 in. tall and of magnificent physique, he was a notable figure in any gathering of men. The son of George Parbury, of Bickley Park, Kent, he was educated at Uppingham. We know little of his scholastic or athletic prowess there, for who is there now remaining who can tell us of a man who was born in 1865? But we know that he was a keen cricketer and that in later years he was a very successful player of tournament tennis. From Uppingham he went to Woolwich to become a soldier, but while he was there his father died and left him a comfortable independence. This may have unsettled him. At any rate he decided to change his profession, and partly, perhaps, from the influence of his uncle, who was surgeon to Queen Victoria, entered St. Bartholomew's Hospital to study medicine. There, though he stayed for several years, this restless, active giant could not be contained. He had already reached the final stages of his studentship when he fell violently in love with a charming young lady, married her at short notice, abandoned his studies, and went careering off on a round-the-world honeymoon cruise. Arriving at New Zealand, he was so captivated with the country that he decided not to return to Bart's. He bought a sheep farm, and there he stayed for ten years, and there the first three of his children were born.

But the urge to medicine had never really left him, and after doing some work at Otago University he sold his farm (now in the possession of Sir Sidney Holland, late Premier of New Zealand) and returned to Bart's, where he qualified M.R.C.S., L.R.C.P. in 1901. He was then 36 years of age, and he went into general practice at Sharnbrook, a village near Bedford. But general practice soon became irksome to so independent a nature, and in 1910 he took the D.P.H.(Cambridge) and was appointed medical officer of health to several rural districts in Bedfordshire. Then came the first world war, and in 1914 his military instincts quickly took him back into the Army—not this time into the cavalry, but, pushed by his qualification, into the sanitary section of the R.A.M.C.

He retired as a major and returned to Bedfordshire, but in his wanderings in France he had seen something of *x*-ray work, rather primitive though it was in those days, and he decided that here were fresh worlds to conquer. In 1922 he took the D.M.R.E.(Cambridge), and after a period as clinical assistant at Bart's he started practice as a radiologist in Bedford and was appointed the first honorary radiologist to Bedford County Hospital and later to Kettering General Hospital. While continuing to live at Sharnbrook Grange he bought for his private *x*-ray practice a house in Bedford's "Harley Street," where he installed genuine deep *x*-ray apparatus in the front room and diagnostic apparatus in the back. At the same time, since radiology was then still only an adolescent science, he continued some of his work as a rural medical officer of health. He was chairman of the Bedfordshire Division of the B.M.A. in 1923–4.

It is odd to think in these days of grace that in the 1920's, and in some cases even later, there was no full-time radiologist in either Bedfordshire or in any of four neighbouring counties. Even in the large industrial town of Northampton, where in a vigorous department the *x*-ray work is now shared by four busy radiologists, it was then the part-time province of a consultant physician. In Bedford it was probably in *x*-ray therapy that Parbury did his best work. He was a born pioneer who would have nothing but the most powerful apparatus, and given wider opportunities he might have done great things. Those were the days before shock-proofing had come in, and H.T. sparks were apt to fly from place to place, but Parbury was quite unperturbed; and if a naked cable activated at 220,000 volts seemed a little close, he just tied it back with a piece of string. In diagnostic radiology he was probably a little less interested, or perhaps, already in his sixties, he felt that it was growing too fast for him, and in 1932 he decided to retire from this branch of his work and hand over to a full-time radiologist, while keeping on some of his work as a rural district medical officer of health.

It is a long time now since he retired from Bedford Hospital, and most of those with whom he was associated have now passed on, but echoes of him still remain. Though genial and good-natured, he was, as radiologists sometimes are, a very forthright man, and he could not abide officials. The story is probably a true one that on one occasion, irritated beyond endurance by one who did not like his paper-work, he seized the unfortunate fellow, himself a big man, by the seat of his trousers and the collar of his coat and hurled him into the passage. *Sic transit gloria mundi.* What would he have done in these days of nationalized committees and controls?

Parbury could not be idle, and he kept on his work as a medical officer of health all through the second world war until 1946, when he was 80 years of age. Earlier this year, when he was 93 years old, he survived a major operation, and when the writer of these notes met his wife a few days after he had returned home she had just had great difficulty in keeping him indoors because he wanted to go and see the gas people, who, he was assured, had overcharged him. To the last he was gardening and carpentering and in the evenings playing bridge, at which, on the night before he passed suddenly and peacefully away, he took a shilling off each of his opponents. Parbury was married three times. His first wife, Ann Lilian Crouch, died in 1926; his second, Muriel Osborn, died in 1936. To his widow, who was Muriel Sale, and who for the last twenty-one years of his life gave him unceasingly gentle yet unobtrusive care, the family owes a great debt. Five daughters survive him, and all of them helped him at some time in his practice, especially the youngest, who is Miss Kathleen Parbury, the world-famous sculptor. There are nine grandchildren and four great-grandchildren.

W. J. C. SYMONDS, B.M., B.Ch.

Dr. W. J. C. Symonds, who had been practising in Toronto for the last five years, died there on April 12. His untimely death at the age of 36 has been a sore blow to his many friends and patients.

After serving during the war as a pilot in the R.A.F., William James Charters Symonds completed his clinical work at Guy's Hospital, where he obtained house appointments in the face of strong competition. In 1953 he emigrated to Canada with his family, where for a time he worked in a life assurance office. However, he soon realized that this was not the life he wished to lead, and set up in private practice, confining himself to medicine. He was not only a doctor of first-class ability, but he also quickly became the trusted friend and confidant of his patients. His practice grew rapidly, and within a short time he was one of the hardest-worked practitioners in Toronto. In spite of this he never spared himself, and was always ready to listen to the problems of his patients and give them kindly and sympathetic advice.—J. J. C.

T. R. L. F. writes: Those who were privileged to know Bill Symonds will feel a deep sense of loss at his untimely death. Bill possessed a truly magnetic personality; his unselfish generosity combined with a courageous spirit and bubbling sense of humour endeared him to all. These qualities were quickly appreciated by his patients and colleagues at Guy's, where many examples of his kindness will be remembered. He had qualified as a fighter pilot in the R.A.F. before coming to Guy's, so as soon as he qualified he volunteered for service in the Royal Auxiliary Air Force and became medical officer to 600 (City of London) Squadron. With them he spent every available moment, flying as often as possible. Many an A.T.C. cadet has cause to be grateful that at his first trip into the air he was piloted by the ever-thoughtful medical officer. Bill's success in Toronto was assured. It was characteristic of him that for many months he had been overworking, and it was this that led to his sudden and totally unexpected death. To his wife, four children, and family we extend our deep sympathy.

E. GORDON CAMPBELL, M.B., B.Ch., D.P.H.

Dr. E. Gordon Campbell, who was in general practice in the West Riding of Yorkshire for 35 years, died at his home at Harrogate on April 1. He was 72 years of age.

Edward Gordon Campbell was born in Tipperary on July 7, 1886, and was educated in Scotland and Ireland, graduating M.A. at Dublin University in 1909. After a short spell as a schoolteacher, during which he played rugby football for Cumberland, he was ordained in the Church of England in 1910, and held curacies in the north and south of Ireland until he entered the Army as a chaplain in 1914 for service in the first world war. He served in Flanders until 1917, when he returned to Dublin, and in the following year re-entered Trinity College as a medical student. He obtained the degrees of M.B., B.Ch. in 1921 and the Diploma in Public Health in 1922. After holding an appointment at the Rotunda Hospital he was granted the diploma of L.M. in 1921. In 1923 he married Clare, daughter of the Rev. James O'Callaghan, and went to Nidderdale, in the West Riding of Yorkshire, to take up an appointment under the Bradford County Borough Council. Some years later he moved to Ripley, and finally to Harrogate, where for

some time he held an appointment as obstetrician and gynaecologist to the General Hospital, in addition to his general practice.—W. K. Y.

D. G. B. writes: Edward Gordon Campbell was a man of outstanding character and ability. He represented all that was finest in general practice, bringing to it qualities that are now unhappily becoming rare. He was an extremely modest and sensitive man, and though he built up a large and successful practice in Harrogate and the surrounding district he was essentially a man of the country, happiest among his country patients or, when on holiday, walking among the mountains and lochs of the Western Highlands he loved so well. As I look back over nearly 24 years of close and valued friendship, I remember him best as a man of infinite wisdom. All who sought his counsel were rewarded by help and advice of solid worth. He had little use for the ersatz of much of modern life, though a kindly good humour gave him tolerance. "Cammy" was a wonderful man who will be missed by all who knew him, and who will never be replaced. He served his day and generation supremely well.

CARL HUPPENBAUER, M.D.

Dr. Carl Huppenbauer, for many years ophthalmologist to the Government of the Gold Coast (now Ghana), died in Germany on April 25 at the age of 75.

M. P. B. writes: Born in Agogo, in the Gold Coast, Carl Huppenbauer was the son of German missionaries. His mother developed white leg when he was born, and it was feared she would die. Runners were sent to Accra for ether, and her leg was amputated by one of the missionaries who was not a doctor. Carl was christened on his mother's coffin, which had been made in the anticipation of her death. His father was suffering from blackwater fever at the time, and it was feared that he also would die. In fact, both his parents survived, and further children were born to them. Carl was sent to Germany to study medicine, and graduated M.D. at Tübingen in 1912. About 1924 he returned to West Africa, and built his own mission hospital at Hohoe, in Togoland. In 1939, on the outbreak of the second world war, he was detained in Accra, but was allowed to work at Korla Bu Hospital. From 1939 to 1956, when he retired, he was ophthalmic specialist to the Government. His great friend was Dr. Harry Chenard, with whom he stayed in Kumasi for six months before finally returning to Germany. They continued to write to each other weekly, and it is a remarkable coincidence that these two friends should have died on the same day. Carl Huppenbauer was a great man and a fine doctor, and he will long be remembered in Africa, where he was so well beloved by all who knew him. Our sympathy is extended to his widow and daughters.

A. H. CHENARD, M.R.C.S., L.R.C.P.

Dr. A. H. Chenard, who was a member of the Colonial Medical Service for some years, died in his sleep at Kumasi, Ghana, on April 25. He was 53 years of age.

Arthur Henri Chenard de la Giraudais was born in the Seychelles in 1905. He studied medicine at Charing Cross Hospital, qualifying M.R.C.S., L.R.C.P. in 1932, and then holding resident appointments at Queen Charlotte's Hospital and the Chelsea Hospital for Women. In 1938 he entered the Colonial Medical Service and was posted to the Gold Coast (now Ghana) as a medical officer. About 1950 he was invalided out of the service and went into private practice in the Channel Islands. On the death of his wife in that year he returned to Ghana as a teacher at the midwifery training school, and four years ago he entered private practice, this time in Kumasi.

M. P. B. writes: The untimely death of Harry Chenard, who was a gifted gynaecologist and obstetrician, will have come as a shock to all who knew him, both in Ghana and in Europe. He had a most charming personality and will long be remembered by all who met him, both socially and professionally. At his bungalow in Kumasi he indulged his hobby of gardening, and he loved to write to his many friends scattered round the world. To his nephew and family sincere sympathy is extended.

D. F. BARRETT, M.B., B.Ch.

Dr. D. F. Barrett, who had been in general practice in Huddersfield for over 25 years, died suddenly at his home there on May 11.

Daniel Francis Barrett was born in Dublin on December 3, 1902. He studied medicine at University College and the Mater Hospital, Dublin, and graduated M.B., B.Ch. in 1927. After gaining extensive experience of general practice as assistant in different towns in the West Riding of Yorkshire he acquired a practice in the Fartown district of Huddersfield in 1933. Ably assisted by his wife, he soon had one of the largest practices in the district. Always a hard worker, he had a flair for general practice. His easy, friendly approach to his patients and to his colleagues, his quick understanding of their problems and his sound advice thereon, added to clinical acumen of a high order, rapidly made him known and appreciated. He followed his predecessor in the practice, Dr. J. Taylor, as medical officer to the famous Huddersfield Rugby League football club, and with his usual enthusiasm became a keen student and follower of the game, travelling with the club to many of their triumphs in league and cup.

When he went to Huddersfield he became divisional surgeon to the Huddersfield central division of the St. John Ambulance Brigade and gave the movement his customary loyal and zealous support, lecturing and examining in many places. During the second world war he did much work as group superintendent surgeon. Since 1952 he had been area surgeon (south-west area) of the West Riding. He was invested as an Officer Brother of the Venerable Order of St. John of Jerusalem by the Lord Prior of the Order, Lord Wakehurst, in 1958.

Since 1954 he had been a member of the Huddersfield executive council and served on the finance, medical services, and vacancies committees, and in 1955 became chairman of the area committee of the National Hospital Service reserve. When first stricken in October, 1957, by the illness which was later to cause his sudden death he was president-elect of the Huddersfield Medical Society, but was never fit to take up his office during that year. After months of illness, borne with exemplary patience and most marked consideration for his nurses, he was able to take up once more his practice work and outside interests. It was a great happiness that he was once again able to serve others and to carry on his life's work. At the time of his tragic demise he was chairman-elect of the local Division of the British Medical Association.

M. L. K. writes: I first met Frank (as he was always known to his innumerable friends) at our first day school in Dublin. We found each other again in the same class year at University College. After graduation we lost touch until I went to Huddersfield in 1934 and received a warm welcome from him. Ever since I have been grateful for his friendship in the fullest sense of everything that word implies. Frank added golf to his many interests just before the war and was one of the keenest and best-loved members of the Huddersfield golf club. He became a very sound and dependable long handicap player, and, when a rabbits' section was formed, he was the obvious choice as its first captain. His name is commemorated by the handsome silver Barrett bowl, donated by him and competed for annually by the section.

A staunch Catholic, he was a founder member and soon president of the Huddersfield Catenian Circle, which always received his enthusiastic support in its activities. To his devoted wife, Dr. Christian D. H. Barrett, and his two sons, Dr. David Barrett, recently qualified, and the Rev. Michael Barrett, S.J., we all tender our sincere sympathy in their great loss.

Medico-Legal

HOUSE-SURGEON FOLLOWING INSTRUCTIONS NOT NEGLIGENT

[FROM OUR LEGAL CORRESPONDENT]

On March 25 the House of Lords gave judgment dismissing an appeal by the father of James Terris Junor, now aged 12, from a judgment of the Court of Session by which Dr. Evelyn Mary McNicol and the Inverness Hospitals Board of Management were absolved from charges of negligence (*The Times*, March 26).

On July 2, 1953, James Junor, then aged 6, fell off a gate at his parents' farm some 26 miles (42 km.) from Inverness, fracturing his left forearm. The district nurse, who happened to be in the neighbourhood, bathed the arm in "dettol," straightened it, and applied a splint. James was taken by car to the Ross Memorial Hospital at Dingwall, where his arm was *x*-rayed and again splinted, and he was sent on to Raigmore Hospital, Inverness, where he arrived at about 4 p.m. The orthopaedic department at Raigmore Hospital comprised two units each with a consultant and a house-surgeon. A senior registrar supervised both house-surgeons and the day-to-day treatment of patients, but when he was on leave, as he was that month, his duties devolved upon the respective consultants.

Fracture "Potentially Compound"

On admission James was seen by Dr. McNicol, who was then one of the house-surgeons. She reported to Mr. R. W. C. Murray, the consultant of her unit, who in the absence of the registrar was supervising her, that she had James in the other room with a fractured arm and a little wound in the skin. She was worried about the wound and asked what she should do about it. Mr. Murray diagnosed a greenstick fracture of both bones of the forearm, "potentially compound," by which he meant that the little wound might communicate with the fracture, and he therefore told the mother that James would have to stay in hospital for three days for penicillin treatment. Dr. McNicol did not hear this, and was instructed to reduce the fracture. House-surgeons at Raigmore were not allowed to reduce compound fractures by themselves, and Dr. McNicol had never done so, so that she interpreted her instructions as a direction to treat the fracture as simple. She did not understand that Mr. Murray intended James to be kept in hospital for three days for penicillin treatment. Dr. McNicol accordingly reduced the fracture on the same evening, and, being concerned about the danger of infection, she administered half a million units of penicillin while James was in the theatre, together with anti-tetanus serum, and gave verbal instructions for penicillin treatment to be continued in the ward.

Next day Dr. McNicol was asked if James might be discharged. She examined him fully, was satisfied with his condition, and authorized his discharge with instructions that he should return in four weeks for examination. His mother collected him that afternoon.

Amputation for Gas Gangrene

On July 5 James was readmitted to hospital, where his arm had to be amputated at the shoulder because of a severe *Clostridium welchii* gas gangrene infection involving the whole arm. After ten days, during which his condition was critical, he ultimately recovered.

The case against Dr. McNicol was that she had failed in her duty to take normal and reasonable precautions against infection by giving proper and normal penicillin treatment and to continue penicillin treatment until the danger of infection was past. It was said that she was in charge of the case from the beginning; that if the consultant instructed her to treat James's fracture as a simple fracture she ought to have known that the instructions were wrong; and that if without the consultant's instructions she administered penicillin she ought to have given a full course.

In his judgment the Lord Chancellor said that no doubt a mistake was made in letting James leave hospital when he did, but the question was whether Dr. McNicol had exercised the care and skill of a prudent house-surgeon—that is, of a comparative beginner. It was the house-surgeon's duty to carry out the instructions of the consultant unless they were manifestly wrong, and that was Dr. McNicol's primary duty. Where instructions were manifestly wrong, duty and common sense combined to say that they must not be followed. But, in view of the opinion which had been conveyed to Dr. McNicol, it was not an occasion on which she should have disregarded what she believed her instructions to be.

The case against the Board of Management was simply that they were vicariously responsible if Dr. McNicol was negligent, so that the finding of no negligence against her disposed of the claim against them also. If liability had been established the damages awarded would have been £5,000.

LADY HOARE AND THE LONDON CLINIC

[FROM OUR LEGAL CORRESPONDENT]

On May 4 the Court of Appeal delivered judgment in the case of the London Clinic Ltd. Trustees *v.* Hoare (*The Times*, May 5). At first instance, before Mr. Justice Gorman, the London Clinic Ltd. claimed £73 as the balance of fees outstanding for the treatment of Sir Reginald Hoare, Lady Hoare's husband, and Lady Hoare counter-claimed for damages, claiming that the plaintiffs had been negligent in the nursing services they had provided and had thereby shortened her husband's life. Lady Hoare had paid 170 guineas out of a total bill of £240.

Prescription on Wrong Card

Lady Hoare had two principal complaints against the London Clinic. The first arose out of certain errors on the clinic's records. On July 15, 1954, Sir Reginald's doctors visited him in the clinic and prescribed certain drugs. The prescription was written on Sir Reginald's prescription card. That afternoon another doctor visited a patient in the room opposite Sir Reginald and prescribed "pitressin" for her; but in some way or another he wrote this prescription on Sir Reginald's card. Sir Reginald's prescription card must have been left in the wrong room. When the mistake was discovered, either that day or the next, a nurse cut the pitressin prescription off Sir Reginald's card and pinned it to the correct card. It was not proved that Sir Reginald was ever given the pitressin prescribed.

Lady Hoare's second principal complaint concerned an oxygen cylinder. For years Sir Reginald had kept an oxygen cylinder by his bed because it comforted him when he was breathless. During his last week-end in the clinic this cylinder was removed from his bedside, though it was said that there was one in the corridor and he could have had it had he asked for it.

Sir Reginald left the clinic on July 20, 1954, and died shortly afterwards on August 12.

Mr. Justice Gorman found that the clinic had not been negligent, and gave judgment for the clinic for the balance of their fees.

Clinic Not Negligent

The Court of Appeal affirmed the finding that the clinic had not been negligent. The clinic had not fulfilled the high standard required of it, but there was no evidence that Sir Reginald had been injured in any way by the mistakes in the records or by the withdrawal of the oxygen cylinder. However, because the clinic had not carried out to the full their contractual obligations they could not expect to be paid in full. The court held that Lady Hoare had paid enough, and accordingly reversed the judgment awarding the clinic the balance of the fees.

This case illustrates neatly how one's contractual duty to a private patient may be higher than the general duty in tort.

Medical Notes in Parliament

QUESTIONS IN THE COMMONS

Consultants in Scotland

Mr. WILLIAM ROSS (Kilmarnock, Lab.) asked the Secretary of State for Scotland on May 12 how many consultants there were in the Health Service in Scotland at the latest date; how many of these were full-time, and how many part-time; and what were the respective figures for 1952, 1954, 1956, and 1957. Mr. J. NIXON BROWNE, Under Secretary, Scottish Office, gave him the following details: At December 31, 1958, there were 370 whole-time consultants and 425 part-time consultants. There were also 143 consultants who were university staff: most of these were whole-time staff. The comparable figures for 1952, 1954, 1965, and 1957 were:

	Whole-time	Part-time	University
1952	268	378	104
1954	328	394	113
1956	365	413	136
1957	367	426	141

Poliomyelitis in Scotland

Mr. S. VIANT (Willesden, West, Lab.) asked the Secretary of State on May 13 how many persons over 21 years of age had contracted poliomyelitis in Scotland during the last 20 years; how many of the cases had been paralytic; and how many had died from poliomyelitis. Mr. J. S. MACLAY provided the figures for age 25 and over, as figures from age 21 were not available. No distinction could be made between paralytic and non-paralytic forms of the disease, as separate notifications were only required in Scotland from January 1, 1959. The following table contains the information.

Year	Confirmed Notifications of Poliomyelitis (All Forms)	Deaths Due to Poliomyelitis (All Forms)
1939	9	3
1940	2	—
1941	7	7
1942	3	4
1943	5	4
1944	13	3
1945	5	8
1946	6	8
1947	155	30
1948	22	7
1949	25	5
1950	96	24
1951	48	12
1952	26	7
1953	35	1
1954	51	9
1955	62	11
1956	29	6
1957	21	6
1958	71	11

Deaths may occur in a year other than that in which the case was notified.

Coroners' Courts

Mr. P. RAWLINSON (Epsom, Con.) asked the Home Secretary if he was satisfied that the power of coroners to commit for trial should be retained; and if he would introduce legislation to limit this power. Mr. R. A. BUTLER said he could hold out no prospect of introducing legislation on this subject, which raised difficult and complex issues at the present time.

Convictions for Driving Offences

Mr. C. ROYLE (Salford, West, Lab.) asked the Home Secretary on May 14 if he would give the percentage figures for 1958 of the convictions recorded in cases of driving under the influence of drink or drugs, in magistrates' courts and quarter sessions, respectively. Mr. BUTLER said he regretted that figures for 1958 were not yet available. In 1957, 91% of these offences dealt with summarily in magistrates' courts resulted in convictions. Strictly comparable figures for cases coming before courts of quarter session were not available, but 48% of persons tried at courts of quarter session and assize were convicted.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 16** (No. 19) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	1	0	0		4	0	2	0	2
Dysentery	1,067	93	322	7		771	74	193	7	2
Encephalitis, acute	2	0		0		6	1		0	
Enteric fever:										
Typhoid	4	1	6	0		4	0	1	0	
Paratyphoid	3	1	5(B)	0		7	1	2(B)	0	3(B)
Food-poisoning	244	70	10	0		159	32	15	3	
Infective enteritis or diarrhoea under 2 years				10					11	25
Measles*	18,195	719	445	424		3,572	349	170	50	3
Meningococcal infection	24	3	11	1		16	3	6	1	1
Ophthalmia neonatorum	23	7	12	0		23	2	4	0	
Pneumonia†	336	18	198	9		304	34	181	23	2
Poliomyelitis, acute:										
Paralytic	19	7	1	} 1		{ 13	2	} 2	2	7
Non-paralytic	16	4	2			{ 7	1			
Puerperal fever‡	223	41	7	0		220	29	9	1	
Scarlet fever	997	46	86	20		706	53	71	28	12
Tuberculosis:										
Respiratory	567	94	88	15		565	57	89	21	
Non-respiratory	71	12	14	1		67	5	23	2	
Whooping-cough	611	28	84	22		652	21	61	7	22

DEATHS	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	4	1		1		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	3	0	1	5	0	0	0	1
Influenza	23	0	0	3	1	19	1	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				1	0		
Pneumonia	500	36	16	20	12	434	30	25	10	9
Poliomyelitis, acute	3	1		0	0	1	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	} 65	{ 5	4	0	5	} 82	{ 3	5	2	2
Non-respiratory		1	0	0	1		1	1	0	1
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	341	31	26	6	6	306	26	43	3	16
Deaths (excluding stillbirths)	9,626	725	558	128	161	9,005	723	545	90	147
LIVE BIRTHS	15,289	1310	132	282	468	14,792	1227	1132	243	365
STILLBIRTHS	334	18	19			288	12	23		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
‡ Includes puerperal pyrexia.

Vital Statistics

Week Ending May 16

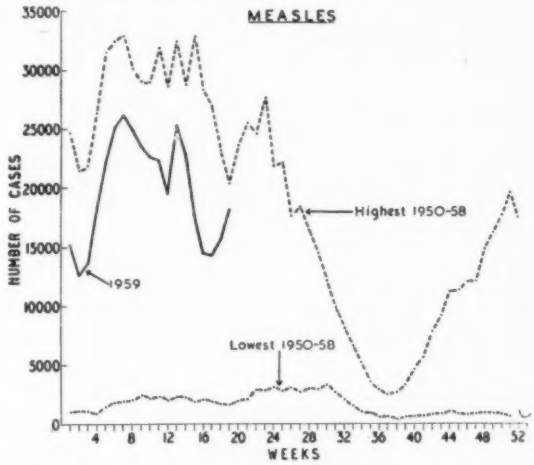
Infectious Diseases

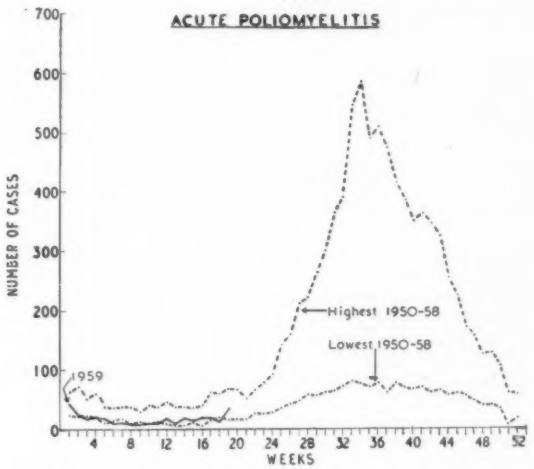
Areas where numbers of notifications were high in the latest two weeks for which figures are available.

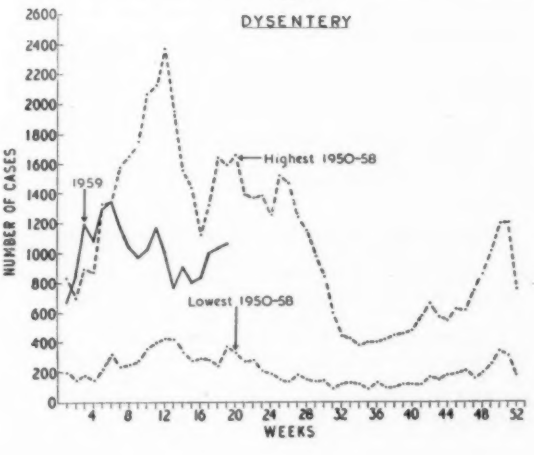
	Week Ending May 9	Week Ending May 16
Measles		
Buckinghamshire	223	**299**
Eton R.D.	2	**101**
Cambridgshire	184	**204**
Cambridge M.B.	81	**115**
Cheshire	450	**548**
Crewe M.B.	119	**161**
Lancashire	1,755	**1,660**
Liverpool C.B.	96	**157**
Lancaster M.B.	90	**120**
Leicestershire	144	**263**
Hinkley U.D.	45	**139**
Middlesex	387	**587**
Potters Bar U.D.	39	**119**
Norfolk	147	**272**
Norwich C.B.	38	**114**
Staffordshire	684	**957**
Stoke on Trent C.B.	107	**215**
Wolverhampton C.B.	52	**114**
Surrey	528	**730**
Croydon C.B.	142	**147**
Warwickshire	680	**868**
Birmingham C.B.	339	**430**
Yorkshire West Riding	1,627	**1,796**
Bradford C.B.	136	**160**
Leeds C.B.	234	**273**
Glamorganshire	265	**262**
Cardiff C.B.	88	**133**
Dysentery		
Essex	40	**49**
Southend-on-Sea C.B. ...	5	**14**
Lancashire	182	**191**
Accrington M.B.	3	**22**
Church U.D.	1	**10**
Heywood M.B.	3	**10**
Lincolnshire	33	**45**
Spilsby R.D.	0	**21**
Northants	3	**21**
Daventry M.B.	3	**20**
Surrey	53	**56**
Croydon C.B.	6	**13**
Bagshot R.D.	6	**19**
Yorkshire West Riding	94	**131**
Bradford C.B.	13	**20**
Caernarvonshire	0	**14**
Conway	0	**14**
Glamorganshire	43	**55**
Cardiff C.B.	14	**18**
Rhondda M.B.	21	**27**
Meningococcal Infection		
Warwickshire	4	**10**
Birmingham C.B.	3	**10**
Acute Poliomyelitis		
London A.C.	2	**11**
Islington M.B.	1	**6**
Hampshire, Southampton C.B. ...	0	**2**
Typhoid Fever		
Fife County	0	**6**

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ------, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Scotland in 1958

The preliminary report for 1958 shows that the birth rate in Scotland was 19.2 per 1,000 population and was 1.0 above the five years' average. The infant mortality rate was 28 per 1,000 live births and was the lowest rate recorded in Scotland, being 1 below the rate for 1957. The neonatal death rate was 19 per 1,000 live births and was also the lowest recorded. The death rate was 12.0 per 1,000 population; this was 0.1 above the rate for 1957 and 0.1 above the average.

Deaths from the principal infectious diseases included 143 from influenza, 25 from meningococcal infections, 4 from whooping-cough, 4 from measles, and 1 from typhoid fever. There were 16 deaths from acute poliomyelitis. Deaths from tuberculosis numbered 638 from the respiratory system and 49 from other forms and were 26 and 10, respectively, fewer than in the preceding year. Deaths attributed to violence included 435 suicides, 629 caused by road transport accidents, and 1,109 caused by accidents in the home; these were 15, 44, and 49, respectively, more than in 1957.

In the fourth quarter of 1958 the birth rate was 19.3 per 1,000 population and was 1.7 above the average of the five preceding fourth quarters. The infant mortality rate was 27 per 1,000 registered live births and was 2 below the rate in the fourth quarter of 1957. The death rate was 11.9 per 1,000 population, being 1.2 lower than the rate in the preceding December quarter but the same as the average for the five preceding December quarters. The deaths from tuberculosis numbered 182 from the respiratory system and 12 from other forms, and these were 25 and 7, respectively, fewer than in the corresponding quarter of the preceding year. Deaths from the principal infectious diseases were 22 from influenza, 8 from meningococcal infections, and 2 from measles. In addition there were 9 deaths from acute poliomyelitis. Of the 709 deaths from violence 276 were attributed to accidents in the home and 173 to road transport accidents.

Medical News

Edinburgh G.P. Centre. — On June 1 the Family Doctor Centre, at Livingstone House, Candlemaker Row, Edinburgh, was opened for work. Its object is to provide diagnostic facilities for general practitioners in Edinburgh. Doctors will be able to bring any patient to this centre whom they would like to investigate more fully than their surgery hours and facilities would normally permit. A suite of fully equipped examination-rooms is available, and rooms can be booked in advance. There is a laboratory for haematology, biochemistry, and a limited amount of bacteriology. *X*-ray and E.C.G. facilities are also provided. The full-time staff comprises an administrative secretary, secretary-typist, nurse, laboratory technician, radiographer, and a medical social worker. A radiologist will attend on a sessional basis. Dr. W. A. ALEXANDER is the honorary medical adviser. The centre will be open initially from 9 a.m. to 5.30 p.m. on weekdays, except Saturday. This new venture has been made possible by the generosity of the Nuffield Provincial Hospitals Trust. Further details may be obtained from the centre's committee of management.

Royal College of Obstetricians and Gynaecologists.—At the meeting of council on May 23, under the chairmanship of the president, Professor A. M. CLAYE, the following were elected to fill statutory vacancies on the council. *Representing the Fellows.*—London: Mr. H. G. E. ARTHURE; England and Wales (excluding London): Mr. W. HAWKESWORTH and Mr. H. J. MALKIN; Scotland: Dr. H. R. MACLENNAN; Northern Ireland and Eire: Dr. N. McI. FALKINER. *Representing the Members.*—England and Wales (excluding London): Dr. DOROTHY SHOTTON; Scotland: Dr. M. M. GARREY. Dr. T. F. CORKILL, of Wellington, New Zealand, was appointed Sims-Black travelling professor for 1960 to visit the British Isles.

The following were admitted to the Fellowship:

B. H. Anderson, S. J. Aptekar, H. R. Arthur, S. Bender, B. E. Blair, G. J. C. Browne, J. E. S. Carmichael, D. G. W. Clyne, J. B. Cochrane, S. J. Cohen, J. McD. Corston, D. Crichton, G. L. Daly, J. A. Davidson, L. M. Edwards, H. H. Francis, I. T. Fraser, S. N. Gardé, F. G. Geldenhuys, B. W. Grieve, W. J. Hamilton, R. L. Hartley, J. R. E. James, W. F. Joynt, J. Karnicki, R. A. H. Kinch, K. I. Liebert, E. W. Little, J. L. Macarthur, J. M. McBride, I. MacGillivray, J. S. MacVine, A. M. D. Milne, C. R. Morison, N. F. Morris, J. Murray, N. Noble, D. L. Poddar, L. J. Quinn, T. F. Redman, R. X. Sands, K. G. Seager, M. J. L. Stening, E. M. Terry, P. C. Thomas.

The following were admitted to the Membership:

E. Aldous-Ball, K. R. Barnes, S. L. Barron, K. Bose, J. A. C. Brown, E. M. Carey, K. Chatterjee, K.-K. Chow, S. Cohen, K. V. Cooper, M. Dass, G. M. Davidson, B. H. Dawson, S. Devi, R. D. Dickinson, P. Dissanayake, P. M. Elliott, R. G. Emerson, B. N. Foy, R. D. Fraser, I. C. Hain, J. J. Handler, S. Haroon, J. G. Harrington, S R. Hazra, M. Howett, R. F. Hutchings, S. A. Martyn, B. Mehra, J. J. Morrissey, H. Mukheiber, S. H. P. Nanayakkara, I. Orr, R. J. Ostolosky, J. F. O'Sullivan, K. D. Printer, M. A. Pugh, S. Ramaswamy, C. M. Rant, A. L. Reynolds, J. N. Rodrigo, M. Rohatgi, R. W. Shannon, D. H. Stewart, W. S. H. Tow, M. A. Wignall.

Medical Research Council Awards.—The Medical Research Council has awarded the following travelling fellowships in medicine to be held in the United States of America in the academic year 1959–60:

Rockefeller Travelling Fellowships: Mr. H. L. DUTHIE, senior registrar and lecturer, department of surgery, Glasgow University; Dr. I. P. C MURRAY, registrar in medicine and endocrinology, Royal Infirmary, Glasgow; Dr. M. M. PLATTS, J. G. Graves Research Fellow, department of medicine, Sheffield University; Dr. J. D. POLLIT, chief assistant, department of psychological medicine, St. Thomas's Hospital, London; Dr. K. B. TAYLOR, assistant to the Nuffield Professor of clinical medicine, Oxford University; Dr. L. G. WHITBY, registrar in chemical pathology, Postgraduate Medical School of London. *Lederle Travelling Fellowship:* Dr. G. R. TUDHOPE, lecturer in therapeutics, Sheffield University. *Alexander Pigott Wernher Memorial Travelling Fellowship in Ophthalmology and Otology:* Dr. A. B. LEITH, resident, Montreal General Hospital, to the Institute of Ophthalmology of the University of London; and Mr. A. N. GRIFFITH, registrar to E.N.T. Department, St. Bartholomew's Hospital.

Scottish Appointments.—Mr. T. D. HADDOW will succeed Mr. JOHN ANDERSON as Secretary to the Department of Health for Scotland on August 1. Mr. Haddow is an Under Secretary in the Department at the moment. Mr. A. B. TAYLOR has been appointed Registrar-General of Births, Marriages, and Deaths in Scotland in place of Mr. E. A. HOGAN, who retired at the end of last month.

B.M.A. Film Competition, 1959.—To encourage the production of good medical films, the Council of the B.M.A. offers two prizes of 50 guineas each (with certificates) for 16 mm. medical films, to be submitted in open competition. One prize is for commercial and the other for non-commercial film producers. In addition, awards of merit will be made where appropriate. Competitors are free to choose their own subjects. Only films completed after September 30, 1957, may be entered for the competition. Further details and entry forms are obtainable from the Secretary, B.M.A. House, Tavistock Square, London, W.C.1. The closing date for receipt of films and entry forms is September 30, 1959.

Royal College of Surgeons.—At a meeting of the council on May 14, under the chairmanship of the president, Sir JAMES PATERSON ROSS, Mr. E. D. AHERN, of Brisbane, and Dr. JOHN H. GIBBON, of Philadelphia, were admitted to the honorary fellowship. The Lady Cade medal was awarded to Squadron Leader T. C. D. WHITESIDE for his research on the effect on visual performance of dazzle from sources of very high brightness, and the Begley prize was awarded to Dr. G. S. MAKIN, of Liverpool University.

Royal College of Physicians, Edinburgh.—The College has awarded the Freeland Barbour Fellowship to Mr. A. F. ANDERSON.

Institute of Almoners.—Representatives of the Institute have been meeting, under the chairmanship of Sir ALLEN DALEY, with representatives of the Royal Colleges of Physicians, Surgeons, Obstetricians and Gynaecologists, and of the College of General Practitioners to discuss the contribution of social work to medical care. In a joint statement stress is laid on the need to re-examine the duties traditionally undertaken by the almoner's department, and on the need for facilities for postgraduate study for almoners.

Leeds University.—Professor A. DURWARD, who holds the Chair of Anatomy, has been appointed Pro-Vice-Chancellor for the sessions 1959–61. Mr. F. E. HOPPER has been appointed to the Chair of Dental Surgery and head of the Dental School from October 1, 1959. Dr. C. J. E. WRIGHT has been promoted to senior lecturer in the department of pathology.

Aberdeen University.—Mr. D. R. INMAN, of University College London, has been appointed lecturer in physiology, starting next January. Miss F. I. G. VINE has been appointed assistant in clinical chemistry.

British Paediatric Association.—Dr. E. W. HART has succeeded Dr. P. R. EVANS as honorary secretary of the British Paediatric Association, whose address is c/o The Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, London, W.C.1.

Royal College of Nursing.—Miss M. J. MARRIOTT, matron of the Middlesex Hospital, has been re-elected president for 1959–60.

Professor Robert Platt, P.R.C.P., has been elected an honorary member of the Association of American Physicians.

Dr. J. D. Sutherland, medical director of the Tavistock Clinic, is to serve on the committee of inquiry into the probation service announced by the Home Secretary, Mr. R. A. BUTLER, earlier this month.

COMING EVENTS

University of Sheffield.—A refresher course for general practitioners will be held during the week beginning September 28. Inquiries and applications should be addressed to the Dean of the Faculty of Medicine, the University, Sheffield, 10, as soon as possible. (See advertisement p. 70 of this week's *Journal*.)

First Emily Blake Memorial Lecture.—Dr. JOE V. MEIGS, of Boston, will lecture at the Medical School, King's College, Newcastle upon Tyne, June 9 at 5 p.m. His subject will be "The Surgical Treatment of Cancer of the Cervix."

Faculty of Radiologists.—Annual meeting, June 19 and 20, at the Royal College of Surgeons. Professor W. V. MAYNEORD will deliver the Skinner Lecture on "Some Problems in the Metabolism of Radioactive Materials in the Human Body." Details from the secretary of the Faculty, 47, Lincoln's Inn Fields, W.C.2.

Society for Endocrinology. — Annual lecture: "A Canadian Trail of Medical Research," by Professor CHARLES H. BEST, F.R.S., at the Royal Society, Burlington House, London, W.1, at 5.30 p.m. on June 23.

British Association of Paediatric Surgeons.—Sixth annual meeting, to be held in Liverpool, June 24 to 26.

Eleventh Ciba Foundation Lecture.—Professor PASTEUR VALLERY-RADOT will lecture (in French) on "Le Rôle de l'Intuition dans la Recherche Médicale" at 5 p.m. on June 26 at the Royal Institution, 21, Albemarle Street, London, W.1. Tickets (free) from the Ciba Foundation, 41, Portland Place, London, W.1.

Institute of Dermatology.—Semi-permanent exhibition on leprosy, until June 30.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, June 6

NORTH-EAST METROPOLITAN THORACIC SOCIETY.—At Honey Lane Hospital, Waltham Abbey, 10.30 a.m., Dr. J. D. Stevens: Bronchial Carcinoma in Women; 11 a.m., Dr. E. G. Sita Lumsden: Dysphagia Pneumonitis.

●ROYAL COLLEGE OF NURSING: PUBLIC HEALTH SECTION.—At Cowdray Hall, Royal College of Nursing, 10.15 a.m., Open Conference on the Report of the Working Party on Social Workers in the Local Authority Health and Welfare Services. Speaker, Mr. R. Huws Jones, M.A.

Monday, June 8

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 4.30 p.m., Mr. A. Gunn: Use of Kielland's Midwifery Forceps.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. B. Ackner: Alcohol Addiction.

Tuesday, June 9

HEATHERWOOD ORTHOPAEDIC HOSPITAL.—8.30 p.m., Mr. G. V. Osborne: Compression Lesions of Peripheral Nerves.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. D. Pond: Use of Tranquillizers in Dermatology.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Mr. D. Fraser: Prolapse and Stress Incontinence.

MIDDLESEX HOSPITAL.—At Clinical Lecture Theatre, 4.15 p.m., Sanderson Wells Lecture by Lord Rt. Hon. Boyd-Orr, F.R.S.: Food, Health, and Politics.

NORTH OF ENGLAND COUNCIL OF BRITISH EMPIRE CANCER CAMPAIGN.—At Medical School, King's College, Newcastle-upon-Tyne, 5 p.m., Emily Blake Memorial Lecture by Dr. Joe V. Meigs (Boston): Surgical Treatment of Cancer of the Cervix.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Mr. Aleck Bourne: Hypertension in Pregnancy.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. G. C. Knight: Treatment of Cervical Spondylosis.

Wednesday, June 10

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. C. Wells: Histochemistry of the Skin.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. W. D. W. Brooks: Treatment of Pneumonia.

LEBANON HOSPITAL FOR MENTAL AND NERVOUS DISORDERS.—At Winter Garden, Cora Hotel, Upper Woburn Place, W.C, 6 p.m., 60th annual meeting.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Professor P. B. Medawar: Some Recent Advances in Immunology.

Thursday, June 11

HONYMAN GILLESPIE LECTURE.—At Anatomy Theatre, University New Buildings, Edinburgh, 5 p.m., Mr. C. W. A. Falconer: Ulcerative Colitis.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. H. Haber: Uncommon Skin Tumours. 5.30 p.m., Dr. I. Macalpine: Application of Psychiatry to Dermatology—Theoretic Aspects.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. E. F. Scowen: Congenital Abnormalities of Adrenal Secretion.

ROYAL SOCIETY OF HEALTH.—2.30 p.m., discussion: Neglected Children, paper by Dr. Doris Odlum.

Friday, June 12

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. C. Wells.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. N. R. Barrett: clinical demonstration.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Dr. F. Avery Jones: Ulcerative Colitis.

Saturday, June 13

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Radiotherapeutic Centre, Addenbrooke's Hospital. Postgraduate courses for general practitioners. Symposium on the place of Radiotherapy in the Treatment of Cancer. *Morning*, 10.15 a.m., Professor J. S. Mitchell, F.R.S.: Introduction to Radiotherapy; 11.15 a.m., demonstration of patients and methods by Dr. Diana Brinkley, Dr. D. G. Brotherton, Dr. D. S. Murrell, Dr. E. M. Kingsley Pillers, and Dr. P. T. Chopping. *Afternoon*, 2.15 p.m., Dr. D. G. Bratherton: Cancer Education; 3 p.m., Professor J. S. Mitchell, F.R.S.: Some New Methods and Ideas in the Treatment of Cancer; 4 p.m., discussion.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Anderson.—On May 10, 1959, at Law Hospital, Carluke, Lanarkshire, Norman Eric Wilson Anderson, M.B., Ch.B., D.P.H., D.T.M.&H., of Lawside, Park Place, Lanark.

Armstrong-Dash.—On May 8, 1959, Charles James Armstrong-Dash, M.D., of 8, Winchelsea Court, Worthing, Sussex, formerly of Addlestone, Surrey.

Barrett.—On May 11, 1959, Daniel Francis Barrett, M.B., Ch.B., of 292, Bradford Road, Fartown, Huddersfield, Yorks, aged 56.

Bednar.—On May 8, 1959, at 13, York Avenue, Hove, Sussex, Marcel Bednar, M.D.

Brown.—On May 10, 1959, Alexander Middleton Brown, M.D., D.P.H., of 77, Park Grove, Westbury-on-Trym, Bristol.

Delahunty.—On May 5, 1959, Patrick Joseph Delahunty, M.B., B.Ch., of Yiewsley, Wolverton, Bucks.

Gunn.—On May 9, 1959, at Edinburgh, David Gunn, M.B., Ch.B., of 22, Orchardhead Road, Edinburgh, late of Loanhead, Midlothian.

John.—On May 7, 1959, David Vernon John, M.R.C.S., L.R.C.P., of Woodmancote, Felinfoel Road, Llanelly, Carm.

Joyce.—On May 8, 1959, in hospital, London, Francis Joyce, M.B., B.Ch., of 115, Denmark Hill, London, S.E., formerly of Dublin.

Moxon.—On May 4, 1959, at 50, Grove Avenue, Sheffield, Yorks, Peter Brearley Moxon, M.B., Ch.B.

Newman.—On May 1, 1959, in hospital, Enfield, Middlesex, Harris Eli Newman, M.D., of Boscombe, Hants, aged 73.

Tait.—On May 3, 1959, at Western General Hospital, Edinburgh, James Herkes Tait, M.B., F.R.C.S.Ed., of 9, Elcho Road, Longniddry, East Lothian, aged 33.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Treatment of Tuberculous Cervical Adenitis

Q.—*What treatment is advised for tuberculous cervical adenitis?*

A.—Many surgeons believe chemotherapy to be of little value in tuberculous cervical adenitis, except perhaps to protect against a spread of infection when operative measures are being undertaken. On the other hand, Miller[1] and Lincoln[2] consider that chemotherapy is useful. There is general agreement that surgical measures are necessary and chemotherapy of no avail when a gland is softening or fluctuant. The type of operative procedure is also a matter of opinion, some surgeons believing that nothing less than block dissection of the neck is required, while others prefer to incise caseous glands and express the contents. Furthermore, some believe that tonsillectomy is indicated in the majority of cases and others that it is needed only if the usual indications (apart from the tuberculous adenitis) are present.

It is probably fair to say that general measures are of the first importance. These include rest, good food, fresh air, and especially control of associated pyogenic upper respiratory infection. Recovery may then follow without the use of antibiotics and without the need for surgery, provided that none of the glands shows signs of softening. In the latter case a course of antibiotic therapy may still be justifiable in the hope that it will help the adenitis to settle down to an extent that will make necessary only the limited measure of incision of individual glands and expression of the contents. Miller[1] considers complete recovery without softening of a gland or glands sooner or later to be exceptional.

There can be no real objection to the use of chemotherapy if conservative measures are contemplated; there is reasonable evidence that it may be of value. The drugs used are isoniazid, and P.A.S. or thiazosulphone. The two former are usually used in conjunction, and it has been demonstrated that a higher blood level of active isoniazid is obtained when P.A.S. is administered concurrently. Isoniazid may be given orally in doses of 10–20 mg. per kilogram of body weight daily, with a maximum of 400 mg. daily. P.A.S. may be given orally in amounts of 0.5 g. per kilogram daily, with a maximum of 12 g. daily. They should be given in 3 or 4 doses at 4-hourly intervals. P.A.S. may cause anorexia, nausea, and vomiting. Thiazosulphone is given orally, initially in amounts of 0.5 g. per day divided into 4 doses. The quantity is then increased until sufficient is given to produce a blood level of 1–3 mg. per ml. 2½–3 hours after the dose is given. Control by estimating the blood level is necessary at first owing to the frequency of toxic symptoms (leukopenia, haemolytic anaemia, and vomiting) if these figures are exceeded.

REFERENCES

[1] Miller, F. J. W., in *Recent Advances in Paediatrics*, 1958, edited by D. Gairdner, 2nd ed., p. 279. Churchill, London.
[2] Lincoln, E. M., *Advanc. Pediat.*, 1958, **10**, 96.

Infective Hepatitis from Oysters

Q.—*Can the infective agent of acute infective hepatitis be carried by salt-water shellfish?*

A.—Only one recorded instance comes to mind of the agent of infective hepatitis being carried by salt-water shellfish. An explosive outbreak of hepatitis involving some 600 cases occurred in Scandinavia in December, 1955, and was traced to oysters as vehicles of the infection. Sven Gard[1] refers to the outbreak in a recent publication.

In the same publication Melnick[2] refers to an epidemic in Delhi in November, 1955. In this case raw sewage entered the river downstream from the water intake, but, owing to tidal currents and other factors, sewage flowed upstream, producing heavy contamination of the drinking water. Clinical hepatitis was observed in 2% of a population of 2 million. Other water-borne epidemics have also been reported.

REFERENCES

[1] Gard, S., and Alin, K., in *Hepatitis Frontiers*, 1957, Henry Ford Hospital, Detroit, Michigan, International Symposium, p. 169. J. and A. Churchill, London.
[2] Melnick, J. L., ibid., p. 211.

Boiling Babies' Bottles

Q.—*Assuming a normal standard of care and hygiene, is there any need to boil babies' bottles between feeds?*

A.—It is obvious that a baby's bottle and teat must be boiled before every feed to ensure that they are sterile. The hypochlorite method of sterilizing is equally effective, provided that it is carried out scrupulously as recommended in the textbooks and as advised by the makers of "milton." In homes and institutions, where there are several babies, sterilization between feeds is necessary. In the ordinary home with only one baby the bottle is commonly not boiled at every feed, but merely thoroughly washed. This is probably sufficiently safe, at all events in a country such as Britain, where the tap-water may reasonably be expected to be sterile or virtually so. The virtue of boiling the bottle each time is that it is then certain that no organism will be transferred to the baby through the bottle. The same applies to the teat. The hypochlorite method of sterilizing provides almost equal safety, although there are more possibilities of an error in technique. There is a good deal to be said for the method of terminal sterilization of feeds and for making up all feeds at the beginning of the day for those families who can afford to lay out the money on sufficient bottles for the day and who have a refrigerator or some place in which the prepared feeds can be kept cool.

First Shoes

Q.—*When should an infant with normal feet start wearing shoes, and what type of footwear should be worn?*

A.—An infant with normal feet starts to wear shoes when he needs them—i.e., when he starts walking on hard ground or a floor. The shoes are protective in the avoidance of injury, but there is no time when it can be said that an infant should wear shoes. If the shoe is big enough and has a straight inner border it is largely immaterial whether shoes or boots are worn. In either case a small heel is more comfortable.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Emergencies in General Practice (26s. 9d.).
Refresher Course for General Practitioners, Volumes 2 and 3 (26s. 9d. each).
Clinical Pathology in General Practice (22s. 3d.).
Any Questions?, Volumes 2 and 3 (8s. 3d. each).

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